EXHIBIT L

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION,	MDL NO. 2875
THIS DOCUMENT RELATES TO: Duffy, et al. v. Solco Healthcare U.S., L.L.C., et al., Case No. 1:18-cv-15076-RBK-JS	

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Veritext Virtual Zoom Videotaped deposition of MAHYAR ETMINAN, Ph.D., taken on Tuesday, August 24, 2021, held in Vancouver, City of British Columbia, Canada, commencing at 8:00 a.m., before Jamie I. Moskowitz, a Certified Court Reporter and Certified Livenote Reporter.

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REQUEST PAGE

INSTRUCTIONS NOT TO ANSWER:

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None	

REQUEST FOR PRODUCTION OF DOCUMENTS:

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None		

STIPULATIONS:

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None	

QUESTIONS MARKED:

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None	

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THE VIDEOGRAPHER: We are going on the record at 8 a.m. on August 24th, 2021. This is Media Unit Number 1 of the video recorded deposition of Mahyar Etminan in regards to the valsartan, losartan litigation.

My name's Justin Bily from the firm Veritext and I am the videographer. The court reporter is Jamie Moskowitz from the firm Veritext. All counsel will be noted on the stenographic record. Will the court reporter please swear in witness and then we can begin.

* * *

P R O C E E D I N G S

THE COURT REPORTER: The attorneys participating in this deposition acknowledge that I am not physically present in the deposition room and that I will be reporting this deposition remotely.

They further acknowledge that, in lieu of an oath administered in person, the witness will verbally declare his testimony in this matter is under penalty of perjury.

The parties and their counsel consent to this arrangement and waive any objections to this manner of reporting. If there are any

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objections, please state them now.

* * *

MAHYAR ETMINAN, after having been first duly sworn, was examined and testified as follows:

* * *

THE COURT REPORTER: Okay, please proceed.

EXAMINATION BY MR. GALLAGHER:

Q Good morning, Dr. Etminan. You can put your hand down now.

A Good morning.

Q My name is Patrick Gallagher. I'm with the law firm of Duane Morris. I represent some of the defendants in this matter, and I'll be asking you a series of questions today for your deposition. Can you please state your name for the record?

A Mahyar Etminan.

Q Dr. Etminan, have you ever been deposed before?

A Yes.

Q How many times?

A Just off the top of my head, at least four or five times.

Q Okay. When did you first speak with

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plaintiffs' counsel with respect to this case?

A Again, to the best of my recollection, I believe it was probably in late spring, maybe April or May.

Q Okay. And who was that counsel that you first spoke to about this case?

A Again, it was either Mr. Nigh or Ms. -- I forget her last name. Rosemarie.

Q Okay.

A I don't -- I'm not sure exactly which one posed the question, but they both approached me.

Q Okay. And have you ever spoken to either -- either Mr. Nigh or Rosemarie prior to speaking to them about this case?

A I did some work for them on a different litigation as well.

Q Did you serve as a testifying expert?

MR. NIGH: Hold on. Don't answer that question. We have not disclosed experts in Zantac, so I'm not going to allow him to answer any more questions about the Zantac litigation.

MR. GALLAGHER: Okay.

BY MR. GALLAGHER:

Q Other than this case, have you had other -- strike that.

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Have you spoken to any other experts involved in this case, the valsartan litigation?

A No.

Q Okay. Have you reviewed any -- have you reviewed any expert reports of other experts with respect to this litigation?

A Yes, I have reviewed Dr. Prizing, I believe, and their reports.

Q Okay.

MR. GALLAGHER: Can we mark the first exhibit Exhibit 1? It's the deposition notice.

(Whereupon, Exhibit 1 was marked for Identification.)

MS. APPEL: It's already marked.

BY MR. GALLAGHER:

Q Dr. Etminan, have you seen this document before?

A Yes.

MR. GALLAGHER: And if we go to the -- I think it's on the next page, next page.

BY MR. GALLAGHER:

Q Have you -- did you review this?

MR. GALLAGHER: Then we can skip ahead to the next page.

THE WITNESS: Yes, I have.

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BY MR. GALLAGHER:
Q Do you see there's a series of requests for certain documents? Did you -- did you collect documents to -- to be produced in response to these requests?
A Yes.
MR. NIGH: And for the record, we did serve response to his requests on defense counsel more than 48 hours prior to this deposition.
MR. GALLAGHER: We did receive -- receive those documents.
BY MR. GALLAGHER:
Q How did you go about collecting the documents that you provided in response to these requests?
A I provided all documents, pertinent studies that I used to formulate an opinion in my expert report, including my search strategy and, again, the articles that I found that sort of contributed to the weight of the evidence that I used in my report.
Q Okay. And with respect to the articles that you provided in response to the request, how did you -- how did you decide what

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articles you were going include and provide?
A Again, the articles where I talked about extensively in the report, that contribute substantially to the weight of the evidence, I have included all of those articles.
Q Okay. Did you have like a file of these articles, or was -- were you --
A Well, I had --
MR. NIGH: Form. Objection.
THE WITNESS: I -- I -- my report is mainly a systematic review of the literature. So when I did my systematic review, I found articles that met the selection criteria in that review. So I went ahead and completed the report. And when I received this request, I went back and looked at all the -- the main articles or studies that I have included. And I went about selecting them again, using mainly the criteria in my research, in my search and also the weight of the evidence that they contributed to the report.
BY MR. GALLAGHER:
Q So I think that -- the documents that -- or the articles -- strike that.
The articles that you provided in

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response to these requests, include some of the articles and papers that are cited in your report but not all of the articles and papers that are cited in your report.
MR. NIGH: Hold on, Doctor. Doctor, hold on. Hold on. If you can, let Patrick finish his question. I know it may be a little difficult because it sometimes does sound like he trails off at the end. But at the same point, I need a pause in between his question and your answer, so I that I can, you know, interject an objection if I -- if I need to.
So here, I'm going to object to form.
Go ahead, you can answer, Doctor.
THE WITNESS: Yeah, so if there were citations in the report where I only looked at the abstract of the paper and not really included the body of the paper because I didn't need to, those articles are just cited in my report. But I provided the articles that actually contributed to the weight of the evidence and my opinions in the report.
BY MR. GALLAGHER:
Q So would it be fair to say, then, that articles that are cited -- that may be cited in your

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report but that you did not provide in response to these requests did not contribute to your opinions in this matter?
MR. NIGH: Form. Objection. Misstates his testimony.
You can answer.
THE WITNESS: No, they do. Again, if -- if there was -- if there were statements that I made that are general statements that are -- that are sort of known facts, I, you know, didn't really provide those specific articles. But I cite them. I provided articles where I, you know, make a lot of discussions around the weight of the evidence provided in those articles.
BY MR. GALLAGHER:
Q Okay. Let's move on and mark as Exhibit 2 your CV.
(Whereupon, Exhibit 2 was marked for Identification.)
THE WITNESS: Sorry. Is this going to be a document upload or is it --
BY MR. GALLAGHER:
Q It is.
A I'm still waiting.

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MR. NIGH: Yeah, we don't have it yet. There it is. Do you have it, Doctor?
THE WITNESS: I got it, yeah.
BY MR. GALLAGHER:
Q So Dr. Etminan, you're an associate professor in the Department of Ophthalmology and Visual Sciences; is that correct?
A That's right.
Q At the University of British Columbia, correct?
A Correct.
Q What does that position entail?
A The position is mainly 60, 70 percent research position. And the 30 or 40 percent remainder is basically -- basically, it's made up of teaching, graduate and undergraduate training and a few hours a month of service.
Q And when you refer to service, what do you mean by "service"?
A Service means attending committees, departmental meetings, that sort of thing.
Q Okay. And in your teaching, what courses do you teach?
A Currently, I teach a two-hour course on evidence-based medicine and with a -- with a

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focus on causal inference to pharmacy students. I also teach a similar lecture to graduate students in the department of ophthalmology. And another pharmacy course on evidence-based medicine, with -- one is undergraduate, and one is for the pharmacy residents who have graduated. But it's two different courses but same sort of topic: evidence-based medicine.
Q Okay. And I believe you mentioned in the 30 to 40 percent, you said teaching and graduate, undergraduate training. Is there any aspect of graduate or undergraduate training you're referring to other than the courses you teach?
A Right. So I teach undergraduate medical students, and it's more of a -- sort of a research rotation, if you will, that they have. So they spend six to eight weeks reading up on epidemiological methodology and taking on a project. I do some -- the same sort of research teaching as well to ophthalmology residents.
And then I have also graduate students who are enrolled in a master's or a Ph.D. program through the Department of Experimental Medicine, and I supervise them on sort of a more regular basis because they're -- you know, they're graduate

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students working toward a master's or a Ph.D.
THE COURT REPORTER: I'm sorry. You -- they have a master's or Ph.D. through the Department of Experimental Medicine? I'm sorry, I missed what you said.
THE WITNESS: Yes, so experimental medicine is a department where all faculties of school -- all faculties who are researching in the faculty of medicine can train students through the Department of Experimental Medicine. So it's like an academic hub, if you will, to -- for graduates training in the -- in the faculty of medicine.
MR. NIGH: And, Doctor, if Jamie speaks up -- or Ms. Moskowitz, if she speaks up, she just wants to clarify what words you used at the end of a sentence. Patrick is going to be the one asking you questions about like what is that type of thing. Okay?
THE WITNESS: Okay.
BY MR. GALLAGHER:
Q Dr. Etminan, in the -- you referred to graduate and undergraduate students. Do you teach medical students?
A Yes, I teach undergraduate medical

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students. I also have started teaching, as I mentioned to you, undergraduate pharmacy students as well.
Q How long have you been a professor at the University of British Columbia?
A Since 2008.
Q And where were you immediately before you started at the University of British Columbia?
A Before -- I held a research associate position at Vancouver General Hospital. Before I was, you know, I started my professorial position, I worked as a research associate for 2 or 3 years at Vancouver Hospital.
Q Okay. And, Dr. Etminan, you received a PharmD degree from Idaho State University; is that correct?
A That's right.
Q Did you do your -- did you attend any other universities for a PharmD program?
MR. NIGH: Form objection.
THE WITNESS: Yes, I -- I started my PharmD at the University of British Columbia, but I completed it at Idaho State University.
BY MR. GALLAGHER:
Q And so how many years did you -- what

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year did you start the PharmD program at the University of British Columbia?
A I believe it was in 1999, or actually 1998 or 9, I forget. And I did one year at UBC, and then I transferred and completed my degree at Idaho.
Q Okay. Why did you transfer?
A I felt that the program, it does not really state my, sort of, objectives, which were more research, pharmaceutical research in epidemiology. It was a more of a clinical program, so I completed it -- Idaho allowed me to finish my degree faster and then go ahead and continue my training in epidemiology.
Q Okay. And then after your PharmD, you went to the University of Toronto; is that correct?
A That's right.
Q And what was the program you were enrolled in at University of Toronto?
A It was a master's degree in clinical epidemiology.
Q Then looks like subsequently, you did a postdoctoral fellowship at McGill University; is that correct?
A That's right.
Q What was the nature of your work

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during that postdoctoral fellowship?
A I undertook epidemiological studies on prescription drugs, safety questions using launch databases or big data.
Q Did any of those studies involve the study of cancer?
A No, not -- not during my training at McGill. I wasn't -- no. Or at least I don't remember. I have done a lot of studies. I don't think one of my studies at McGill had anything to do with cancer.
Q Okay. Jumping ahead to -- as we discussed just a few minutes ago, you're a professor in the Department of Ophthalmology and Visual Sciences, correct?
A That's right.
Q And I think you said 60 to 70 percent of your time was -- was research?
A That's right.
Q What's the primary -- what's the primary focus of your research currently?
A My primary focus of my research again is sort of broken down to 40 to 50 percent epidemiology of the eye or ocular diseases or drug safety questions related to the eye. And the rest

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of the -- the other 40 to 50 percent is drug safety questions on any other area in -- in medicine. So I worked on drugs related to the lung, to the gastrointestinal tract, any -- anything -- any drug safety question that is of public health concern.
Q How do you identify drugs that you're going to undertake research on?
MR. NIGH: Form objection.
THE WITNESS: Well, it's usually case reports or case series or alerts from drug regulatory agencies. Sometimes the media is a good source to highlight important -- importance of a safety question. So it could be a combination of all of those, or it could be one of them.
BY MR. GALLAGHER:
Q You're not a medical doctor, correct?
A No.
Q And you don't diagnose patients, correct?
A No.
Q You don't treat patients, correct?
A Correct.
Q When I asked you about what you did as a professor in the Department of Ophthalmology and

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Visual Science, you didn't mention anything about clinical involvement. That's not a part of what you do as a professor at the University of British Columbia, correct?
A Correct.
Q I believe you said you -- I believe you have been deposed four or five times; is that correct?
A Correct.
Q Have you ever testified at trial?
A I testified, I believe, in the lower Manhattan court for Fosamax once, yes.
Q Okay. Do you know if your testimony has ever been excluded by a court?
MR. NIGH: Form objection.
THE WITNESS: I'm not sure. It's possible -- possibly Fosamax, but I'm not 100 percent sure.
Q Okay.
THE COURT REPORTER: I'm sorry. What was that? Fosamax?
THE WITNESS: Right. Fosamax. F-o-s-a-m-a-x.
THE COURT REPORTER: Oh, Fosamax. Okay. Thank you.

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BY MR. GALLAGHER:
Q Dr. Etminan, have you ever withdrawn as an expert in this case?
MR. NIGH: Form objection.
THE WITNESS: Yes.
THE COURT REPORTER: I'm sorry .I need the question repeated.
BY MR. GALLAGHER:
Q Dr. Etminan, have you ever withdrawn as an expert in a case?
MR. NIGH: Form objection.
THE WITNESS: Yes.
BY MR. GALLAGHER:
Q What case did you withdraw as an expert?
A It was the Mirena litigation.
Q Why did you withdraw?
A I felt that I could not contribute anymore to the litigation, and I felt more comfortable to withdraw.
Q Dr. Etminan, do you consider yourself to be a statistician?
A I'm not a statistician, but I have good familiarity with biostatistics that pertains to my line of work in the area of epidemiology that

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I -- that I work at.
Q Would you say that you use statistics in your work as an -- as an epidemiologist?
A Yes.
Q Okay. What does the term "statistically significant" mean --
THE COURT REPORTER: I'm sorry. There's -- there's background noise coming in. I'm not sure where it's coming from, but I'm not hearing you well.
MR. GALLAGHER: I'll -- I'll repeat the question.
BY MR. GALLAGHER:
Q What does the term "statistically significant" mean from an epidemiological standpoint?
A Actually, it's -- that's a great question. So for many, believe that the statistically significant means that results of a study are -- for example, if the P value is large and the results are not statistically significant, that means that the -- there is really no effect associated with that -- that exposure, carcinogen.
But in reality, this is really not the case. And the American Statistical Association, in

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2016, published commentary to sort of clear the water on this issue.
So the correct interpretation of your question on statistical significance means that if some -- if an effect size of a -- from a study is not statistically significant, that means that it does not deviate from the statistical model and assumptions that it -- that it carries with it.
It does not have anything -- it does not say anything at all about whether, you know, that particular exposure of a study and the outcome are related or associated. That's -- that's all it means, that the -- the data and the assumptions around that data for that analysis do not deviate.
Q So what does that mean, to say that "the data and the assumptions do not deviate"?
MR. NIGH: Form objection.
THE WITNESS: Again, in more simple terms, when we do a study, there are -- the data that we use. The type of a statistical model that we use carries with it a number of assumptions.
And if -- if the results are statistically significant, all it means is that your data, the data that you have from that

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study, are, if you will, different than -- than -- than the model that you're using, provided that all other assumptions are met.
So it's more about whether the data fits in the assumptions or not. It's not about -- statistically significant means that, yes, this exposure causes this outcome, or if it's not significant, it means it doesn't. That's not what a statistical significant means at all.
BY MR. GALLAGHER:
Q So statistical significance -- are you saying -- what I understand you to be saying is that statistical significance is not evidence of causation?
MR. NIGH: Object to form, mischaracterizes his testimony.
THE WITNESS: Yeah, it's -- statistical significance doesn't have anything to do with causation. Statistical significance, again, means how similar is my data to the statistical model that I'm using provided all other -- all the assumptions that need to be met are met. Sometimes they are not. But do the assumptions have to -- to be

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met, so, again, there are caveats.
It also -- statistical significance also is a reflection of precision as well. Studies with a large sample size are -- are more precise in terms of the -- let's say, the confidence interval around the effect size because there are very large sample sizes. Usually, they have higher events.
Smaller studies with lower sample size and lower events usually have a wider confidence interval or a larger P value because of -- they're -- they're more imprecise. So, again, statistical significance and whether an exposure is causing an outcome are different -- are two different entities.
BY MR. GALLAGHER:
Q In your work, do you have an understanding of the concept of adjusted rate ratio?
A Yes.
Q From your perspective, what is an adjusted rate ratio?
A An adjusted rate ratio is a rate ratios that's been adjusted using statistical modeling for either one other variable, which we call covariate. So it could be age, or it could be

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adjusted for multiple variables.
Q And what's the purpose of doing the adjustment?
A The purpose of an adjustment is to make sure that the two groups exposed -- or, say, the drug group and the unexposed group are balanced with respect to potential confounding variables in -- in a particular study.
However, again, all of these issues have intricacies and nuances. And one of the nuances is that, you know, adjustment for the wrong variable can actually be detrimental as well. So we want to make sure that we adjust for variables that need to be adjusted for.
Q How do you determine what variables need to be adjusted for?
A Well, that's an area that actually I have been working on for the past few years, and I have been advocating. So what one of the -- sort of up-and-coming methods is the use of what we call "causal diagrams" where we draw -- draw out all the common causes of whatever the question is, whether it -- exposure on health that you're looking at. We draw all the common causes for that question, and then we find which -- which are the paths -- what we

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call "biasing paths" that need to be adjusted for or blocked.
MR. GALLAGHER: Let's mark as the next exhibit, Exhibit 3, a paper in which you are an author, you cited in your report titled "Personal Use of Hair Dyes" --
THE COURT REPORTER: I'm sorry, "Personal Use of Hair Dye" --
MR. GALLAGHER: "And Risk of Cancer."
(Whereupon, Exhibit 3 was marked for Identification.)
MR. GALLAGHER: That will be coming up shortly.
BY MR. GALLAGHER:
Q Do you have it, Dr. Etminan?
A Is that Exhibit 3?
Q Yes.
A Yes, I'm just opening it.
Q You're familiar with this paper?
A It's -- it's been a while because it was published a few years back, but yes.
Q Okay. When is the last time you read this paper?
A Many years ago.
Q Okay. It was published in 2005. That

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would probably be the last time you read it?
A Yes.
Q What was your contribution to this paper?
A Again, as the best of my recollection, I helped with the search -- searching of the studies and the write of the manuscript -- write-up of the manuscript, yeah. So I think mostly gathering the evidence and writing the paper up.
Q Would you consider this to be a landmark paper?
MR. NIGH: Form objection.
THE WITNESS: It was -- I'm not sure what you mean by "landmark," but it was, at that time, the first study or review, comprehensive review of the topic.
BY MR. GALLAGHER:
Q If we go to Page 2519, which I think is the fourth page of the document, do you see there's a section here called "Quality Assessment"?
A Yes.
Q What was the purpose of doing a quality assessment?
THE COURT REPORTER: I'm sorry. Doctor, can you start that again, please?

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BY MR. GALLAGHER:
Q What was the purpose of doing a quality assessment?
A The purpose of a quality assessment was to look at the quality of the studies that was included.
Q And it looks like you tried to establish an objective 10-point scale to evaluate the quality of the study; is that correct?
A Let me just read it for a second.
Q Sure.
A So it seems like from the description that we came up with our own sort of a description of a quality assessment. It's nothing that is -- is validated. We kind of improvised based on this -- you know, the type of data that we had.
Q Okay. But you established specific criteria by which the quality of the -- each of the studies that were included was evaluated?
A Yes.
Q Is that correct?
MR. NIGH: Object to the form.
THE WITNESS: Yeah.
BY MR. GALLAGHER:
Q If we go to Page 2523 of the article,

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under -- do you see there's a heading "Comment," the paragraph right under that.
So it looks like the -- in this -- this paper your -- the results indicated that there's no effect of personal hair dye use on the risk of breast and bladder cancer; is that correct?
A Yes.
Q And you concluded, there's a borderline effect for hematopoietic cancers, but the evidence of a causal effect is too weak to represent a major public health concern.
How did you --
MR. NIGH: We couldn't hear you. It just broke up during your question, Patrick.
THE WITNESS: Sorry. Patrick, can you repeat your question? I'm okay.
MR. GALLAGHER: Yes, I will repeat the question.
BY MR. GALLAGHER:
Q How did you decide that the causal effect is too weak?
MR. NIGH: Form objection.
THE WITNESS: Honestly, I -- I don't remember. It's -- it's way back. Could have been just the numbers that we got. I don't

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remember exactly how we decided on the wording of -- of the comment.
BY MR. GALLAGHER:
Q If we go back one page to Page 2522, look at Table 6, which looks like is presenting pooled relative risks of hematopoietic cancers of hair dye use.
THE COURT REPORTER: I'm sorry. Can you repeat that?
BY MR. GALLAGHER:
Q Table 6 is presenting the pooled relative risks of hematopoietic cancers in hair dye use, correct?
A Yes.
Q Are these the numbers that -- that you're referring to that you would have looked at to decide the -- the causal effect is too weak?
MR. NIGH: Form objection. That misstates the -- the evidence of the prior document.
THE WITNESS: Yes. We probably looked at these numbers to come up with a conclusion.
BY MR. GALLAGHER:
Q What does it mean for -- for the relative risk to be --

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THE COURT REPORTER: To be what?
MR. GALLAGHER: One.
THE WITNESS: One means there's no effect. There is no causal link.
BY MR. GALLAGHER:
Q Is the relative risk looking at a causal link or looking at an association?
A Well, again, for the purposes of this paper -- this academic paper, you can use association, if you will. And so a relative risk of 1.0 would be no association.
Q Okay. And then I guess more broadly, the concept of the relative risk generally is looking at an association. It's not determinative of causation, correct?
MR. NIGH: Form objection.
THE WITNESS: No, I disagree with that. A relative risk is just a measure of effect. I mean, if you have -- you could have a relative risk from a very well-designed randomized trial, which is a, you know, true experiment. That relative risk would probably mean, to a high degree of certainty, a causation.
So it's not the relative risk --

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whether it's a relative risk or the odds ratio that's presenting the effect size. It's the study design, and all the other factors that have gone into the study design, and the methodology that would tell you whether you believe the numbers are a causal blame versus an association.

BY MR. GALLAGHER:

Q And so what -- what factors -- how do you determine whether a study is -- is being used to -- to evaluate an association versus being used to evaluate causation?

MR. NIGH: Form objection.

THE WITNESS: So if I'm looking at one study, I look at the methodology, the -- the way -- you know, the type of biases that may have played and whether those biases actually would reverse the direction of the effect side, would change the results or not. If I'm looking at a more broader question, then I am looking at the totality of the evidence.

So again, one study from a journal, I kind of look at it differently than, you know, a real-life broader question, where I have to decide whether the substance causes --

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THE COURT REPORTER: Whether the substance causes what?

THE WITNESS: Whatever outcome that we are looking at.

BY MR. GALLAGHER:

Q If in this article, we go ahead to Page 2524. In the middle column, the last full paragraph starts "The borderline effect." In this section of your paper, you wrote, "The borderline effect observed for brain tumors and ovarian cancer is based on the pooling of only two studies and does not permit a meaningful assessment of the risk."

Do you see that?

A Yes.

Q So you agree that, here, only looking at two studies wasn't -- wasn't sufficient to be able to evaluate the risk of hair dye for development of brain tumors and ovarian cancer, correct?

MR. NIGH: Form objection.

THE WITNESS: I mean, that's what we have. And again, you have to factor in a number of, I think, points. One is that my knowledge in causal inference in 2005 was not the same as it is now, so I may have done

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things differently.

And a lot of what we write in these academic papers is also influenced by the editors who tell us, sort of, what type of wording to use, sometimes.

So, you know, yes, that's what we say here on this specific paper, and that's what was said. But I think there are sort of caveats to that.

BY MR. GALLAGHER:

Q Do you disagree with this statement in your paper?

A I don't disagree that that's what we said. But, again, the specific wording of that statement -- going back, I'm not sure what discussions we had -- could have been also influenced by the editors wanting us to sort of lower the tone, perhaps. Or in this case, you know, it is -- it could have been possible -- I'm not familiar with this area right now, with this area of hair dye and cancers.

But back then, it would have been feasible to say that with two studies, it's not a meaningful risk based on the data that we had then.

Q So you made -- do you believe that the

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editors asked you to change the wording of this specific sentence in this paper?

A I -- I don't know.

MR. NIGH: Form objection.

THE WITNESS: I'm not saying that they did. I'm just saying sometimes in academic writing, if I want to say -- if I believe from my study that this drug causes this disease, at times we are -- we do receive pushback for, sort of, a lighter tone in that -- in presenting that statement.

And I don't know if this happened here or not, but I'm just saying that it's -- it could have been possible that this sentence came up with my contribution, my other authors' contribution and potentially the contribution of other editors as well.

BY MR. GALLAGHER:

Q In your academic work, when you're submitting articles for publication, do you allow editors to change the language of the article that you have written?

MR. NIGH: Form objection.

BY MR. GALLAGHER:

Q To something that you don't agree

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with?
MR. NIGH: Form objection.
THE WITNESS: Well, it's a collective agreement. They make suggestions, and we look at the suggestions. And we agree or disagree. So it's -- you know, it's in -- you know, different situations are different.
MR. GALLAGHER: Okay. We can take this -- take this exhibit down.
Let's mark as Exhibit 4 your invoices.
THE WITNESS: Okay.
MR. GALLAGHER: Which, I believe, they provided -- were provided through the plaintiffs' counsel in response to the document requests.
(Whereupon, Exhibit 4 was marked for Identification.)
MR. GALLAGHER: That will be uploaded shortly.
BY MR. GALLAGHER:
Q Dr. Etminan --
MR. GALLAGHER: If we can go to the last page of this collection of invoices. I believe they are in reverse chronological order.

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BY MR. GALLAGHER:
Q Dr. Etminan, does this refresh your recollection as to when you first spoke with plaintiffs' counsel about this case?
A Yes, probably around those dates, around those dates or maybe a bit before.
Q Okay. Around the time that you first became involved in this case, did plaintiffs' attorneys send you any documents?
A They -- yeah. I mean, they may have sent me some articles on the topic, and then as we went along, there were more documents that I reviewed.
Q Okay. Are -- are some of the articles that they provided to you articles that you cited in your report?
A I mean, I did -- I did my own systematic search. Some of the articles at the end would have -- could have been, you know, also the ones that they may have provided as well. But I didn't go with what they gave me. I went with my -- the articles that came out of my systematic review.
Q Okay. Have you ever seen any of these articles prior to being involved in this litigation?
A I can't recall. I mean, I read a lot

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on different topics.
MR. GALLAGHER: Let's mark as Exhibit 5 a copy of your report.
(Whereupon, Exhibit 5 was marked for Identification.)
BY MR. GALLAGHER:
Q Is it up? Do you have it there?
A Yeah, I have it.
Q Okay.
A Yes.
Q If you go up to page -- let's start at Page 12 of your report.
A Okay.
Q At the bottom, Section 8.1, you talk about a search strategy and study ascertainment. Do you see that section?
A Yes.
Q Is this the search strategy that you were just referring to for your identification of -- of articles?
A Sorry. I lost you there. What was the question?
Q Sure. A few minutes ago, you had referenced, I think you called it a systematic search that you had done?

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A Yes.
Q Is this the search strategy that you are referring to?
A Yes.
Q How did you come up with this particular search strategy?
A Well, I mean, I have done a lot of search strategies for my work, so I -- the question is on the risk of cancer and --
THE COURT REPORTER: I'm sorry -- and what?
THE WITNESS: NDMA.
So I identified the MeSH terms, the medical subject heading terms that would capture NDMA and combined it with cancer, including different types of cancer, and restricted it to epidemiological studies because those are the type of studies that I wanted to look at. So in a nutshell, that was the structure of the search.
BY MR. GALLAGHER:
Q Okay. And then if we go to the next page, Page 13, it's referring to study inclusion and exclusion criteria. Do you see that?
A Yes.

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Q How did you come up with the inclusion and exclusion criteria?
A In order to, again, assess a causation for this question, I needed the studies to have presented some sort of an effect size, like the relative risk or an odds ratio or hazard ratio, have identified the outcome, cancer, and also have -- it has to have measured NDMA because I don't want to mix -- did not want to mix studies that included other carcinogens with NDMA. So that had to be one of the key criteria.
And I think those are the main criteria that I included.
Q Okay. What do you mean when you say you didn't want to use studies that mixed other carcinogens with NDMA?
A Well, you have a lot of studies on diet and processed food that also have looked at cancer that we know that -- for example, you know, red meat that could have NDMA, but it could also have other carcinogens that also contribute to cancer. So I wanted -- I wanted this study to specifically look at NDMA and cancer.
Q Okay. But the -- but the study -- so if the study is looking at red meat, any study that

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is -- is looking at a causal association of dietary intake of red meat and cancer is going to include exposure to other carcinogens, correct?
MR. NIGH: Form objection.
THE WITNESS: Yes. There are -- there are carcinogens in red meat. But my interest is looking at the risk of cancer with the NDMA component. And if the study did not measure NDMA, sort of, separately, then it is very difficult to draw a causal relation between the NDMA and cancer in the meat product or other carcinogens and cancer in the meat product.
BY MR. GALLAGHER:
Q Okay. If you look under "Study Exclusion Criteria," the sentence immediately after the bolded underlined sentence. It says, "Moreover, lack of quantifying or categorizing (low versus high) NDMA/NDEA amounts in these studies will make it difficult to necessarily draw a causal link."
Do you see that?
A Uh-huh.
Q So were you only looking for studies that would support the conclusion of a causal link?
MR. NIGH: Form objection.
THE WITNESS: No, I'm not sure -- I'm

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not clear on your question. So the sentence says, "Studies of meat intake where NDMA was not measured."
Again, if -- if the study is looking at meat and that -- that meat product has NDMA and other carcinogens and they show a risk with cancer, we can never tell what caused the cancer. Was it the NDMA component or the other components? So those studies that did not specify NDMA measurement were excluded.
BY MR. GALLAGHER:
Q Okay. Did you -- did you review or consider studies that were not cited in your report?
A You mean to reach my conclusion in the report?
Q We'll start with it more broadly.
Did you review and consider studies that were not cited in your report?
A I -- I reviewed studies that met my inclusion criteria that were included in my report.
Q So -- but were there -- were there studies that met your inclusion criteria that you reviewed that you haven't cited in your report?
A I don't believe so. If it's not in the report, it's because it didn't have the

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inclusion criteria. For example, it, you know, did not provide odds ratios or relative risks or NDMA levels. That -- I mean, that's -- that's why they were not in the report.
Q Okay. Some of the -- of the papers that you cited in your report are occupational studies, correct?
A Correct.
Q What is "occupational studies"?
A Occupational epidemiological studies are studies that -- that look at risk of, whether it's cancer, or it could be cardiovascular disease, in people who are exposed to an occupational exposure, so -- you know, people working in factories or rubber factories or, you know, hair dye factories. I mean, those would be considered examples of occupational exposure.
Q And the occupational studies that you looked at for your report were looking at people working in rubber factories, correct?
A Yes, the Hidajat studies and a couple of other ones that --
THE COURT REPORTER: I'm sorry. The what studies?
THE WITNESS: Hidajat, spelled

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H-i-d-a-j-a-t.
BY MR. GALLAGHER:
Q And are -- how -- for -- for people working in the rubber industry, how many different carcinogens are they exposed to by virtue of working in a rubber factory?
MR. NIGH: Form objection.
THE WITNESS: They could be different carcinogen exposures.
BY MR. GALLAGHER:
Q Do you have an estimate for how many different carcinogens they're exposed to?
MR. NIGH: Form objection.
THE WITNESS: No, I don't.
BY MR. GALLAGHER:
Q So you don't know -- you reviewed -- you reviewed a few of these occupations studies, but you don't know how many different carcinogens the rubber workers are exposed to by virtue of working in a rubber factory?
MR. NIGH: Form objection.
THE WITNESS: I don't remember --
MR. NIGH: Hold on. Hold on. Let me object to the form first. Form objection.
Go ahead, Doctor.

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THE WITNESS: I don't remember the specific numbers, but I think it's important to know, and I agree with you, that they would be exposed to a -- a number of different carcinogens.
BY MR. GALLAGHER:
Q Okay. In these -- in these occupational studies -- strike that. Let's go ahead and mark them, first.
MR. GALLAGHER: So let's mark as Exhibit 6 the McElvenny article 7 is the Straif article.
THE COURT REPORTER: Is the what article?
MR. GALLAGHER: Straif, S-t-r-a-i-f article.
And Exhibit 8 will be the Hidajat article.
(Whereupon, Exhibit 6 was marked for Identification.)
(Whereupon, Exhibit 7 was marked for Identification.)
(Whereupon, Exhibit 8 was marked for Identification.)
THE COURT REPORTER: Can I take one

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minute? I don't need to go off the record.
Can I take one minute?
MR. GALLAGHER: Why don't we go ahead and go off the record for a minute?
THE VIDEOGRAPHER: The time is now 9:09. This ends Media Unit Number 1. We're going off the record.
(Whereupon, a short break was taken.)
THE VIDEOGRAPHER: The time is now 9:11. This begins Media Unit Number 2. We're back on the record.
BY MR. GALLAGHER:
Q Okay. Dr. Etminan, we have marked as Exhibits 6, 7 and 8 three articles you cited in your report that are all occupational studies.
A Yes.
Q McElvenny paper, the Straif paper and the Hidajat paper. Do you see those?
A Yeah.
MR. NIGH: We don't -- I don't see Number 8 in the Dropbox, in the chat, I mean. There we go. Just came up.
MR. GALLAGHER: Sorry. It was a bit late.

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BY MR. GALLAGHER:
Q And each of these three papers is looking at -- are occupational studies looking at risk of cancer in workers at rubber factories, correct?
A Generally speaking, they are, but they are a little different in terms of the study design.
Q When you say they're a little different, do you mean each of the studies is slightly different from the other study in their study design?
A Well, I mean, the main difference between McElvenny and Hidajat is that McElvenny just looked at cancer with occupational exposure, whereas Hidajat actually teased out the NDMA exposure component, looked at different -- those categories for each cancer, and took a number of methodological steps to reduce potential biases that McElvenny did not do.
Q Okay. You included McElvenny in -- why did you include McElvenny in your report?
MR. NIGH: Form objection.
THE WITNESS: I -- I wanted to also just briefly touch on other occupational studies as well, because if I hadn't, then

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there would be a question of, you know, why did you -- why did you only look at Hidajat. So I wanted to mention that there are these occupational studies as well, but my focus was on the study by Hidajat because it met the main inclusion criteria for my question.
Q Did the McElvenny study -- article, though, meet your exclusion criteria?
A It may have because they did not include NDMA. And again, I just mentioned that it's not in my main analytical framework of evidence when I'm deciding on the causal question. But I just thought to introduce, you know, just to mention it as background that there -- you know -- and it is part of Hidajat -- in a way related to Hidajat. It's an older version of Hidajat, so I thought I should mention it.
Q So you included the McElvenny article in your report even though it met the exclusion criteria for studies that should be excluded?
A Again --
MR. NIGH: Form objection.
THE WITNESS: The -- the -- the inclusion criteria is -- is mainly used to form my opinion, which, again, is included in the

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Bradford Hill criteria and the main, sort of, framework of my opinion on the causal effects. I mention -- I briefly mentioned McElvenny and Straif because they are also other -- the other relatively well-cited occupational exposure cancer studies, and I mentioned them as, you know, background in my -- in the paragraph.
BY MR. GALLAGHER:
Q But I am correct that McElvenny meets the exclusion criteria that you set out for studies that should be excluded?
A Yes.
Q Okay. For these occupational studies, the method of exposure was primarily through inhalation or skin contact. Would you agree with that?
MR. NIGH: Form objection.
THE WITNESS: Yeah.
BY MR. GALLAGHER:
Q Okay. And that method of exposure is different from the method of exposure that's at issue in this case, correct?
A The method of exposure is different, but my -- the question, the general causation question that I -- that my report refers to does not

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specify cause of cancer with NDMA with respect to different rounds of exposure. It refers to, generally speaking, exposure. And we mean systemic exposure, which could be mouth or through the skin or through inhalation cause cancer.
Q Okay. So the question that you were evaluating was not whether NDMA ingested orally could cause certain cancers; is that correct?
MR. NIGH: Form objection.
THE WITNESS: No, that's not -- that's not what I said. The question that I addressed was: Does exposure to NDMA and exposure would mean NDMA that gets in to the body systemic -- systemically absorbed NDMA, which can be through oral, inhalation, skin. I think mainly those are the -- the main routes of the exposure. Does builds -- does exposure to NDMA through any of those routes that make it systemic in the body cause cancer.
BY MR. GALLAGHER:
Q So is -- the question that you were addressing was more broadly, does exposure to NDMA in any manner have an association or potentially lead to cancer; is that correct?
A Any matter that -- that leads to

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systemic absorption. So if I could clarify, so if -- if -- if for -- let's say, hypothetically, there was a study where a person inhaled NDMA for one day, that -- that would not really be systemic absorption of NDMA. But if in a study of a 40-year follow up, people are exposed to NDMA through skin and inhalation, you can be sure that they are, throughout the time of follow up, are getting exposed to NDMA systemically.
Q Okay. Let me unpack that a little bit.
So you're referring to a time frame component?
A Yes, I mean the studies that I included are epidemiological studies. They are -- either follow a patient forward or have asked about their intake. So they -- they have been followed for a time, and these patients have been exposed to NDMA over time.
Q Okay. Do you agree with me that the -- that the method of -- what the method of exposure is to NDMA can have an impact on what tissues in body are exposed to NDMA?
A Can you clarify the question, please?
Q Sure. I guess do you have any

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understanding -- let me ask it this way: Do you have any understanding whether different tissues are exposed to NDMA if the exposure is through inhalation versus through skin contact versus oral ingestion?
A From animal studies, we know that it has caused cancer from those different routes of administration in animals. In humans, again, exposure to NDMA where it gets into your system can affect different organs, just like smoking -- primarily smoking causes lung cancer. But we have evidence that it can also cause other cancers.
So it's not that -- although it's mostly affecting the lung, that the carcinogen is probably affecting other -- other organs as well.
Q Okay. I understand what you're saying, but do you have any understanding whether the method by which a person is exposed to NDMA impacts the tissues that are actually exposed to NDMA?
MR. NIGH: Form objection.
THE WITNESS: You mean like a toxicology study or an epidemiological study that looks at different tissue levels with respect to cancer? Can you, maybe, elaborate a

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little bit about the type of study you're asking about?
BY MR. GALLAGHER:
Q Sure. I don't think I'm asking about a study, necessarily. I'm asking if you have an understanding of whether the -- do you have any understanding whether an exposure to NDMA through oral ingestion versus exposure through inhalation has any differences in the tissues that are ultimately exposed -- ultimately exposed to NDMA?
A No. I mean, I think that's -- that's sort of like a toxicology type of question. I don't know of any details of specific concentration of NDMA in each organ, no.
Q Okay. Let's look at the Straif article that's Exhibit 7.
So in your report, you say -- you say that there with an increase in the risk of --
THE COURT REPORTER: In the risk of -- I'm sorry. In the risk of what?
MR. GALLAGHER: All cancer deaths.
THE COURT REPORTER: I'm not understanding.
MR. GALLAGHER: I'll repeat the question.

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BY MR. GALLAGHER:
Q In your report, you say about the Straif study that there was an increase in the risk of all cancer deaths. And you identify the relative risk of 1.4 with the confidence interval of 1 to 1.8?
A Let me find that, just one second.
Q Okay. If you look at Page 14 of your report.
A Okay. 14, okay. Okay.
Q So you agree that this -- this was not statistically significant?
MR. NIGH: Form objection.
THE WITNESS: I think it just missed the statistical significance because it -- the lower balance starts with 1.0.
BY MR. GALLAGHER:
Q So it did miss the statistical significance because the lower bound of the 95 percent --
THE COURT REPORTER: Can you repeat that, please?
MR. GALLAGHER: Sure.
BY MR. GALLAGHER:
Q Sure. It missed statistical

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significance because the lower bound of 95 percent confidence interval included 1.0, correct?
A Correct.
Q And as we discussed previously, a relative risk of 1.0 means there's no association between the exposure and the risk that's being validated, correct?
A Well, the relative risk is 1.4. The lower bound is 1.0. And, again, it speaks to precision. I cannot -- I cannot exclude this size -- this relative risk of 1.4 and just say it's not -- because it's not statistically significant, there is no harm. Again, I -- I think we spoke about the caveats of interpretation of what the P value is and statistical significance really means.
So I mean, it is a 1.4 relative risk with those confidence intervals.
Q Okay. If you were to present data to a peer --
THE COURT REPORTER: To appear what?
BY MR. GALLAGHER:
Q To a peer-reviewed journal, like this where the confidence interval includes 1.0.
A Uh-huh.

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Q Would you expect that peer-reviewed journal would not let you say that there was statistically significant association?
MR. NIGH: Form objection.
THE WITNESS: Again, it -- it depends on the journal on the editorial board. The statistical significant, sort of, misnomer, if you will, that I talked about, is relatively recent. And the American Statistical Association put out this correction on the interpretation of this -- this topic in 2016. So it will take a while before most editorial boards and editors really come to grasp of what -- what this concept means.
So, again, because up until now, a lot of these editors are sort of interested in statistical significance versus nonstatistical significance. It's possible that some journals still ask that.
BY MR. GALLAGHER:
Q I believe we've talked about this a couple of times now. When you submit an article for consideration to be published in a peer-reviewed journal, there's review by, you call them editors; is that right?

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A There's usually a peer review of two or more peers, external reviewers, and then there is -- yes, there is an editor that also reviews it.
Q And when -- what is the purpose of the peer-review process?
A The peer-review process is to try to ensure as much as possible, and sometimes that does not happen, but the process is there to ensure that the research is -- is vetted and -- and checked before it's published.
Q Okay. And when you -- when you submit an article for the peer-review process, is it sometimes either the peer reviewers or the editors ask you to make changes to the article?
A Yes, usually they do.
Q And part of the purpose of that peer review process and the changes that they may ask for is to improve the scientific accuracy and validity of what's being published, right?
A That is correct.
MR. NIGH: Objection.
BY MR. GALLAGHER:
Q Okay. And the report, Exhibit 5, that you submitted in this litigation, your expert report, that was not submitted through peer review,

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correct?
A No.
Q Looking at the Straif article, Exhibit 7, specifically on Page 181.
A Yes.
Q I'll come back to that later.
MR. GALLAGHER: Let's take maybe a 10-minute break right now.
THE WITNESS: Sure.
THE VIDEOGRAPHER: The time is 9:33 a.m. and we're going off the record.
(Whereupon, a short break was taken.)
THE VIDEOGRAPHER: The time is now 9:47. We're back on the record.
BY MR. GALLAGHER:
Q Welcome back, Dr. Etminan.
A Thank you.
Q If you look at Page 14 of your report, the paragraph about -- where you're writing about the McElvenny article?
A Uh-huh.
Q Is that -- this is Exhibit 5, the -- towards the bottom of that paragraph, you say, "These men might have been exposed to carcinogens other than NDMA and NDEA"?

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A Yes.
Q And, in fact, working in the rubber factories, they probably were exposed to many carcinogens other than NDMA and NDEA, right?
A Yes, possible.
Q And the same would be true for the rubber workers who are study subjects of the Straif article?
A Yeah.
Q And the same would be true for the cohort of rubber workers that were subjects of the Hidajat article, right? Those men would have been exposed to many carcinogens other than NDMA and NDEA, correct?
A If I could clarify, so, yes, all of these men were working in these factories, and they were exposed to a number of carcinogens, including NDMA. However, Hidajat was the only one that actually quantified NDMA in different levels. And if -- if you're inferring that there could be a potential risk of cancer with other carcinogens, that is true. However, we have to actually know that the -- the men who are on the highest NDMA exposure in the Hidajat study are actually exposed more to other carcinogens than the men in the lower

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NDMA exposed group.
In other words, for carcinogens -- for other carcinogens to introduce this bias for measurement in this study, you have to be able to show that the NDMA, the highest NDMA category met were getting -- were getting more exposure to those carcinogens than the control group.
And I don't think -- in other words, there is what we call a differential, sort of, measurement. In other words, it's affecting one group more, that's why we see more cancers. But that's not -- I mean, there's no reason to believe that. This is a large population study in the UK. All these men are in the factory. They are all being exposed to different carcinogens probably at the same rate. I mean, there is no -- there is no reason to believe that the ND -- the highest NDMA group that has -- shows higher cancer rates were also exposed to other carcinogens more than the other -- they were probably exposed at equal rates.
Q. Okay. Well, let's look at the Hidajat studies. That's Exhibit 8.
And if you look at -- first off, let's look at the first page, the right-hand column, the -- the last paragraph starts off -- it says,

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"Exposures vary throughout the rubber manufacturing process."
Do you see that?
A. Yes.
Q. So that's following a list of several potential -- exposures to potential carcinogens that exist in the -- in the rubber factory, and it's saying that the exposures vary throughout the rubber manufacturing process, right?
A. What was your -- the last part of your comment? Sorry. I couldn't hear.
Q. It's saying here that the exposures to these potential carcinogens vary throughout the rubber manufacturing process, right?
A. Yes, they vary, yeah.
Q. And then going to the next page, Page 251, the right-hand column, the top heading, "Exposure Assessment" -- first off, this is looking at a study of rubber workers in the UK, correct?
A. Yes.
Q. The cohort of -- it was male rubber factory workers in the UK aged 35 years or older as of 1 February 1967, and that's on this Page 251 under "Materials and Methods"?
A. Uh-huh.

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THE COURT REPORTER: Is that yes?
THE WITNESS: Yes.
BY MR. GALLAGHER:
Q. So the first sentence under "Exposure Assessment," says, "Exposure assessment was based on estimates from the EU-EX-ASRUB database of measurements of compounds in rubber factories in Europe," right?
A. Uh-huh. Yes.
Q. So this is where they're getting the estimates for each of the compounds that they're looking at, including NDMA, right?
A. Yes.
Q. Okay. And that's citing to Reference Number 18, and if we go forward to Page 258 on the right-hand column, you see Reference 18. And that's an article by DeVocht as the lead author, right?
A. Yeah.
MR. GALLAGHER: Let's mark as Exhibit 9 the DeVocht article.
(Whereupon, Exhibit 9 was marked for Identification.)
MR. GALLAGHER: Let me know when it shows up in the chat.

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THE WITNESS: Yeah, it just showed up.
BY MR. GALLAGHER:
Q. If we go to Page 694 under -- under "Results"?
A. Uh-huh.
Q. And this is explaining that -- well, I guess, first off, this is the article that Hidajat is citing to as the source of the estimates for exposures, including the exposures to NDMA, correct?
A. Yes.
Q. Okay. And under "Results," it's describing the EX-ASRUB database and explaining that "the measurements in the database have been collected from very different sources in the participating countries."
Did I read that correct?
A. That is correct, but they -- they do -- there's statistical modeling that is mentioned in their method. They do correct for a lot of those heterogeneity between country measurements. So I found that modeling quite robust. Not that -- not that it doesn't have -- I mean, every study has limitations, but I found that -- that part of what they did was quite strong in terms of correcting for those differences that we just mentioned of exposure

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in different countries.
Q Who -- who did the corrections that you're referring to?
A Well, they used the random effects, if you look at the -- if you look at the method -- the statistical methods, I believe.
Q Which article are you looking at?
A DeVocht.
Q Doctor, are you referencing -- are you talking about DeVocht, or are you talking about Hidajat?
A No, DeVocht.
Q Maybe let's look on the Page 697, and if we can start -- start in the left-hand column, the bottom paragraph that's going to then carry over to the right-hand column?
A Okay.
Q Do you see that, it says, "Not only the number of collected measurements and the time periods when they were collected differed between the different countries, but large differences were also found in the type of chemical agents collected depending on nationally set priorities and research interests of particular investigators," right?
A I see that.

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Q Okay. Then it goes on to say, "For example, N-nitrosamine measurements were primarily collected in Germany, while in the UK, measurements of rubber process dust and rubber fumes were made."
Do you see that?
THE COURT REPORTER: I'm sorry. While in the UK, measurements of...
MR. GALLAGHER: Rubber process dust and rubber fumes were made.
BY MR. GALLAGHER:
Q Do you see that?
A Yes.
Q So N-nitrosamine measurements were primarily coming from exposures in factories in Germany? That's where the estimates were coming from in DeVocht, correct?
MR. NIGH: Object to form.
BY MR. GALLAGHER:
Q Correct? Am I correct -- the measurements of N-nitrosamine that are being used in DeVocht are primarily collected from rubber factories in Germany?
MR. NIGH: Object to form.
THE WITNESS: Can I have a few minutes just to read this section, if you allow -- if

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you allow me?
BY MR. GALLAGHER:
Q Sure. Sure. Take a minute.
A Okay. So, yes, they do -- they do -- they do list these limitations as you pointed out. However, I mean, one can argue that these limitations could also potentially underestimate the exposure of -- of what they have measured in their study.
And, again, I go back to my original point. You're following -- you have 35,000 men for about -- sorry, 15,000 men for about 40 years. In order to produce results that are a major deviation from the risks that they have shown, you have to be able to actually show that one group was -- had, you know, a major measurement error in other carcinogens or NDMA more than the other group because this is a population-based study.
And there is really no reason to believe that one group had these limitations and the other group did not. It probably occurred non-differentially in both groups over a long period of time.
So yes, as they said, the study does have some limitations. But I think this limitation

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does -- could actually mean the risk could be potentially higher because it's smaller -- perhaps, potentially a smaller quantity of NDMA was measured, so the techniques that they were talking about.
But overall, I think that the study's strengths, sort of, outweigh its limitations. But, I mean, that is a limitation that they discuss.
Q So you say that based on this limitation, they could have -- potentially could have underestimated any potential association, but they are -- based on that limitation -- they also could have overestimated any potential association, right? That's the nature of the limitation?
A Yes, it could go both ways, but I -- I'm more -- again, I go back to my -- I'm more of a stronger believer in the fact that any major deviation from these results requires, you know, a large amount of measurement error over time only in one group and not the other group. Other limitations could perhaps change the effect size, you know, perhaps a little bit. But I don't see a relative risk of three or four, you know, coming down to one or -- or to the left of one. I don't -- I don't see -- without having evidence of any major measurement error going on, I don't see those

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results drastically changing.
Q Okay. You talked about measurement errors. So talking about the Hidajat study, the Hidajat article?
A Yes.
Q This is a cohort of men working in rubber factories in the UK.
A Right.
Q And --
A Right. By "measurement" there, I mean if one group is exposed, as you also agreed because of other potential carcinogens, if one group -- if there is a measurement error in NDMA in one group, say, the high users more than the lower users, or if there is more exposure of other carcinogens in one group versus the other, in the presence of those, there -- there could be a bias introduced.
But we don't have any evidence that in this long-followed-up large-sample study these errors only favored one group, let's say the high NDMA users and not the -- not the other -- not the control group. There is no evidence to believe that. It probably happened equally over time in both groups.
Q Okay. So you're talking about

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measurement error and measurement of NDMA in the Hidajat study.
A And -- and exposure -- and exposure of other carcinogens, which was also brought up --
Q Okay.
A -- as well.
Q I want to talk for just a minute about the measurement of NDMA.
A Okay.
Q Hidajat -- Hidajat is a cohort of workers in rubber factories in the UK, right?
A Yes.
Q Hidajat did not measure the levels of NDMA to which any of -- to which those workers were exposed, right? It was based on estimates from this database, right?
A Correct.
MR. NIGH: Objection.
THE WITNESS: Measuring -- measuring direct NDMA for each subject and following them for 35 years is pretty much impossible, so that's -- that's the approach that they took.
BY MR. GALLAGHER:
Q Right. But Hidajat didn't take any measurements. Hidajat based -- Hidajat based their

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exposure assessment on estimates from the EX-SARUB database.
A Yes, I think we've -- we've agreed on that, yes.
Q Okay. And now we're looking at DeVocht article, and there, the -- the measurements for N-nitrosamine primarily were collected in Germany, right?
MR. NIGH: Form objection.
THE WITNESS: Yes.
BY MR. GALLAGHER:
Q And they say that there were large differences in the time periods and large differences in the type of chemical agents collected depending on nationally set priorities and research interests of particular investigators, right?
A Right.
Q Okay. Further on here in the next paragraph right below that paragraph, it goes on to say in the DeVocht article, "Furthermore, measured concentrations cannot be compared directly between countries because of the differences in sampling devices used to measure exposures," right?
A Yeah. That's what they said, yeah.
Q So that's a further limitation.

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And then -- and then the bottom of this page, it carries over to the next page, they further say, "This makes it difficult to distinguish between actual differences of exposure between countries and differences in the performances of different sampling devices that are known to exist," right?
A Yes.
Q So we don't know that the exposures for N-nitrosamine, for NDMA, or for NDEA that were included in this database from the DeVocht article, are representative of the rubber factory that are included -- the rubber factories in the UK that are included in the Hidajat cohort, right?
MR. NIGH: Object to form.
THE WITNESS: Again, that -- that could -- I mean, I believe this -- we don't. I believe the assumption would be that they are -- I mean, it's Europe -- it's European countries.
If -- if they were using NDMA exposure data from China and applying it to the UK, I would be concerned. But, here, yes, they don't have exact measurements for each country. But again, there has to be a huge difference

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affecting both the high NDMA and the low NDMA groups over 30 years to -- to shift the -- you know, create a major change in the results that Hidajat produced.
BY MR. GALLAGHER:
Q But that's a limitation that DeVocht -- the authors of the DeVocht article are acknowledging in this database, right?
A Yes.
Q Let's go back to the Hidajat article, on the first page of the article right under "Introduction."
A Okay.
Q It says -- starting off the article, first sentence, they say, "Employment in the rubber industry has been concluded to cause cancer by the International Agency for Research in Cancer (IARC)."
Do you see that?
A Yes.
Q Do you have any reason to disagree with that statement?
A No.
Q And, in fact, rubber -- workers in rubber factories in the UK are exposed to a variety of potential carcinogens, right?

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A Yes.
Q And that includes rubber dust, rubber fumes, polycyclic aromatic hydrocarbons, aromatic amines, benzene, all of those, correct?
A Correct.
Q And that exposure is primarily by inhalation or direct contact with skin, right?
A Yeah.
Q Okay. The -- the Hidajat study didn't -- didn't control for all of these potential confounding exposures, did they?
A I wouldn't call them confounders because the specific definition of a confounder is a variable that has to be associated with both NDMA use and cancer. These are mostly risk factors which means that they are mostly causes of cancer.
And again, I go back to my point, major -- if you're inferring that these -- yes, these are all carcinogens. That's what IARC says, and I have -- I agree with what they're saying. But if you're inferring that these carcinogens contributed to the high relative risk of cancer that we see from Hidajat based on the high NDMA levels; again, I go back to my explanation of the type of bias that -- that needs to be created, has to be

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differential, meaning that it has to -- we have to have data, or we have to intuitively think that these chemicals are only affecting the NDMA -- high NDMA category and not the control group. And there's no reason to believe that's the case.
Most probably, just inferring from what we know from the data from -- from the article of the cancer studies, that this long follow up, these -- these other carcinogens probably affect both the high NDMA -- well, it affects everyone in -- in the study, high NDMA group versus low NDMA group.
And when that happens in the epidemiological studies, it usually -- usually is an underestimation of the true effect. In other words, the risk, relative risk is 7, and it comes down to 5 because of this error, this potential contamination in both groups, which we call "non-differential measurement error."
The bias that you, I think, are referring to is a case where all of these carcinogens are only affecting the high NDMA group and not the other group. And that just doesn't -- you know, we don't have any data for that. It doesn't make a lot of sense why that would happen.

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So to answer your question, yes, a number of these carcinogens were present in this -- in this study just because of the nature of the exposure.
But I don't think it would have changed the results that much, because of this presence of other carcinogens. Again, because there is no reason to believe that it affects one group and not the other group.
Q Well, unless you control for these other exposures, you don't know if there's a differential effect or not?
MR. NIGH: Form objection.
BY MR. GALLAGHER:
Q Correct?
A Can you repeat your question, please?
Q Unless you control for these other exposures, you don't know whether there's a differential effect or not?
MR. NIGH: Form objection.
THE WITNESS: Well, I mean, it's -- it's gonna be very difficult to measure for all of these variables. And, again, they're not -- we -- we control for -- we control for mainly confounders. I'm not sure if all of these are

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confounders in the true sense of the term, which is a variable that affects both the outcome and the exposure.

There are mainly risk factors, and risk factors are not -- not controlling for risk factors is not as detrimental as not controlling for confounders.

This is -- this is a very -- you know, it's a very difficult study to execute, and there's no -- there is no way to control for all of those variables. And I'm not -- again, I'm not sure if -- they're not true confounders, I'm not sure -- not controlling for them would affect the results, or at least a direction of the results, that much.

BY MR. GALLAGHER:

Q Okay. Understanding the distinction you're making between exposures to these other potential carcinogens and confounders, let's talk first about these other potential exposures. And we'll talk about confounders in a few minutes.

If the workers in a specific area of the rubber factory in -- in the UK are exposed to rubber fumes, polycyclic aromatic hydrocarbons, aromatic amines and NDMA, and half of those are

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carcinogens and half of them are not, how do you separate which ones are, if you haven't controlled for those different -- for those exposures?

MR. NIGH: Form objection.

THE WITNESS: Again, that's -- that's very difficult to do. And, again, I go back to my previous point: In a large cohort of 15,000 men with 35 years of follow up, you have to show consistently that the other carcinogens is only affecting the high NDMA users, through the 35 years of follow up constantly in order for the effect of -- of other -- the other carcinogens to be reflected in the relative risk. That -- we don't have any data that that's happening. It doesn't make intuitive sense.

It makes sense that these men are exposed to these carcinogens, but in the span of a 35-year follow-up, it's probably affecting both the high NDMA and the low NDMA equally. And when that happens, that actually dilutes the -- the -- the relative risk that you're seeing.

So, again, we don't have -- there's no way to measure all the -- all these agents that

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you mentioned for all these men and follow them for the 35 years. But because I don't believe it's affecting one group more than the other, I don't -- I don't see a major -- this potential limitation leading to a major bias.

BY MR. GALLAGHER:

Q Well, you say you don't believe it's affecting one group more than another, but that's an assumption you're making, right?

MR. NIGH: Object to form.

THE WITNESS: It's not just an assumption. It's -- I mean, it's -- it's based on the -- the information you're given, this is -- this is rubber factory workers, 35 years of follow-up in the UK. And we are not giving -- we are not given any information that, you know, all of a sudden, this cohort, or at least part of the cohort, is exposed to this other carcinogen more, you know, in the high -- especially in the high NDMA group more than the other, the control group.

So I -- I feel comfortable with the assumption because I -- I just can't see any sort of a logical reason as to why that would happen. It's a -- it's a large population

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based study on the same cohort in the same country followed forward for 35 years.

BY MR. GALLAGHER:

Q Can we go for just a minute to your invoices again, which is Exhibit 4, I think? Is that right? Exhibit 4.

And if we look at Page 3 of 5, this is an invoice from May 5th of 2021.

Do you see the -- there's three entries on this invoice. The bottom entry looks like you spent three hours searching for methodologies to control for unmeasured confounding for the Hidajat study. Do you see that?

A Yes.

Q Why were you searching for methodologies to try to control for unmeasured confounding in the Hidajat study?

A Because I wanted to show how robust the -- the results would be in the absence of one uncontrolled confounded.

Q When you're saying you want to show how robust it is, you're assuming that the results are robust, but for unmeasured confounding factors, right?

MR. NIGH: Form objection.

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THE WITNESS: Well, let me put it, then, another way. I wanted to know if there is -- how much change -- how much the results would change when I include -- when I assimilate this unmeasured confounder into the results.
BY MR. GALLAGHER:
Q Okay. And in order to do that, you had to go search for methodologies to control for those unmeasured confounders, right?
A Yes.
MR. NIGH: Form -- form objection.
BY MR. GALLAGHER:
Q It's not something that you -- you had a methodology that you -- you -- that you typically use, yourself, in your -- in your research?
MR. NIGH: Form objection.
THE WITNESS: Can you repeat the question, please?
BY MR. GALLAGHER:
Q You had to go search for methodologies because you didn't have -- you didn't have a methodology that you typically used for this type of looking at potential effects of unmeasured confounders, right?

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MR. NIGH: Form, form objection.
THE WITNESS: No, I -- I used the E-value methodology which I had -- I have used actually before in my -- in my research studies. I just wanted to do another search just to see if there is any newer or perhaps better methodology than the E-value methodology. And I found that there isn't any, so I used the method that I have used, you know, a number of times in the past in my own research.
BY MR. GALLAGHER:
Q Okay. If we look at your report, Page 15?
A Yes.
Q And is this -- is this table part of what you're referring to in terms of looking at the effect of unmeasured confounders?
A Yes.
Q And walking through the table on the left-hand column, you've listed different specific types of cancer, right?
A Yes.
Q And in the middle column, you -- you're listing hazard ratios without unmeasured

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confounder. Where are you getting those numbers from?
A So by using this methodology that's published, if you include -- there is a formula where you include the -- for example, the stomach cancer is 1.72. If you include this in this formula, it tells you how large that unmeasured confounder has to be to eliminate the risk of 1.72.
So you can see for all the other cancers -- all the cancers listed, the -- the magnitude of the effect of that confounder has to be pretty large to reverse the -- the relevant risks on the left-hand column.
Q So I guess -- let me walk through it this way.
The left-hand column, those are -- are reporting hazard ratios that are coming from the Hidajat study; is that right?
A That's right.
Q Okay. And then in the right-hand column is where you're now calculating what -- what the hazard ratio for an unmeasured confounder would need to be in order to take the relative risk in the left-hand column down to one; is that right?
A Correct.

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Q Okay. And Hidajat, they did not directly control for smoking, right?
A They did not, although -- they did not, although they said they simulated smoking data, and the results did not change.
Q They simulated smoking data, but they didn't control for smoking, right?
A No.
Q Would you consider smoking to be a potential confounder?
A So smoking is definitely a risk factor for cancer, and smoking, in order for it to be a confounder, has to also be potentially associated with NDMA exposure. So it could potentially be confounded, yes.
Q Okay. And another potential confounding factor would be family history of cancer?
A Yes, family history of cancer -- again, so the family history of cancer is definitely a risk factor for cancer. Whether people with family history of cancer are more likely to be exposed to NDMA, that, you know, that side of the triangle, I'm not sure it's possible. But then again, for that confounder to introduce bias, it has

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to -- it's dependent on how prevalent that confounder is in that population and how strong the confounder cancer and confounder NDMA relationship is. So just the absence of a confounder does not mean that necessarily the study is biased, if a confounder has to, you know, a number of criteria have to be met for that unmeasured confounder to actually -- as I have demonstrated in my table, to cause bias in the results.

But theoretically, it could be a potential confounder.

Q Okay. And Hidajat did not control for family history of cancer?

A No.

Q Correct?

A No.

Q Are you aware that infection with H. pylori is a potential risk factor for certain types of cancer?

A Again, it is a risk factor but it's not necessarily a confounder, because H. pylori is not really associated with NDMA exposure.

So not having H. pylori is not going to really bias the results because it's not a confounder. It's a risk factor. However, I don't

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really see it as a major bias. Plus, again, it has to be differential between the two groups, even if it were a confounder.

So I don't -- yes, H. pylori was not measured. And it is -- it is a risk factor for mainly actually stomach cancer, but it is a risk factor of cancer. But it's not -- I don't believe it's necessarily a confounder because it doesn't meet the H. pylori NDMA length in the triangle, in the causal triangle.

Q Well, again, unless you control for it, you don't know if there's differential exposure between --

A Well, first -- first of all, it's not a confounder, so even if it's differential or not differential, because it's not a confounder, it should not really change the results. Smoking is a confounder. We talked about it because it satisfies the confounder definition, but H. pylori, you know, at first glance, it seems, like, oh, we should control for it because it's a risk factor for cancer. But it's not really -- it's not really associated with NDMA users. It's a relatively prevalent infection that many people have. So I don't really -- I don't really see how -- not

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measuring H. pylori could really change the results.

Q What's the distinction that you see between smoking and infection with H. pylori, if smoking is a confounder but H. pylori infection is not?

A Smoking is a confounder because it's associated with cancer, and since it's probably associated with NDMA because these are -- rubber factory workers in the '60s and '70s and, you know, that -- that sort of profession. Especially back then, they were probably smokers. So it meets the -- the dual criteria of a confounder.

H. pylori only has one arrow to cancer, but it doesn't really have an arrow to NDMA in any way. It's not really associated with NDMA, so that's why it's only one arrow to cancer that makes it a risk factor and not a confounder.

Q Do you agree with me that if the members of the cohort from the Hidajat study who were classified -- who were classified by them as high NDMA were more likely to have H. pylori infection than the members of the cohort that were classified as low NDMA exposure, if that would skew the results?

MR. NIGH: Form objection.

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THE WITNESS: No. Again, what you're talking about in terms of one group having more than the other is -- again, it's for confounders. So if you have a confounder that's showing up more in one group than the other, that confounder is probably biasing the results, and you have to do an analysis where you stratify by that confounder to make things clean.

H. pylori is not a confounder, and so even if one group had it more than the other, which we don't really believe is the case, would not really change, because it's -- because it cannot change -- it's not affecting the exposure. It's only affecting the outcome. It wouldn't change the results, I don't believe so.

BY MR. GALLAGHER:

Q If there was a difference in the -- in the percentage of the cohort for high NDMA exposure that had H. pylori infection versus the percentage of the cohort classified as low NDMA that had H. pylori infection, you don't think that that would have any impact on --

A The --

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MR. NIGH: Hold on. Hold on. He didn't finish his question.
Did you finish, Mr. Gallagher?
MR. GALLAGHER: I did, yeah.
MR. NIGH: Okay. Form objection.
THE COURT REPORTER: I didn't hear the end of the question, just the very end.
MR. GALLAGHER: Let me rephrase it.
BY MR. GALLAGHER:
Q Dr. Etminan, is it your opinion that if -- if there was a difference in the percentage of the cohort Hidajat classified as high NDMA exposure that had H. pylori infection versus the percentage of the cohort classified by Hidajat as low NDMA exposure that has H. pylori infection, that -- that would not have any impact on the results --
A I --
MR. NIGH: Hold on. Hold on. Hold on. I'm not sure if he's done.
BY MR. GALLAGHER:
Q That would not have any impact on the results of the study?
MR. NIGH: Form objection.
Go ahead, Doctor.
THE WITNESS: Well, I wouldn't say it

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wouldn't have any impact. I would say it would -- it would affect maybe the precision, maybe a relative risk of say 5 to a 4. But it wouldn't reverse the direction of that -- that effect size. It wouldn't take a 4 to a .5, which confounders could -- could do.
This is just a risk factor. So absence of a risk factor could slightly change the precision, but it wouldn't change the direction of the -- of the effect size in Hidajat.
BY MR. GALLAGHER:
Q So you agree it could impact the observed hazard ratio?
A In the -- in the way that I just explained, yes.
Q So if we look at the table, you -- you say it could go theoretically from a hazard ratio of 5 to a hazard ratios of 4 --
A It could -- it could, but it could be even lower because it has -- you know, there's such a huge sample size. But it's possible to affect precision of the -- of the effect size.
Q Okay. So if we look at your table, for stomach cancer, you're showing a hazard ratio

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without a measured -- a measured confounder of 1.782. Why couldn't it go from 1.72 to 1?
A No. I think -- I think you're just -- I mean, that's -- that's speculation. I could also go to 1.4. I'm just making a general statement that because H. pylori is mainly a risk factor, provided that there is a huge differential in the -- in the level in the measurement of H. pylori between the high NDMA group versus the low NDMA group, there could be changing precision of the hazard ratio, but not a -- not a reversal of the direction of the hazard ratio.
Q Okay. Let's look at the Hidajat study, Exhibit 8.
THE VIDEOGRAPHER: Counsel, there's about 10 minutes left on this media unit.
MR. GALLAGHER: Okay. Thanks.
BY MR. GALLAGHER:
Q At Page 251, again, under "Exposure Assessments" --
MR. NIGH: I'm sorry. Why are we having to -- to break for a media? I haven't seen that with any other court reporter.
MR. GALLAGHER: It has happened in the -- in the other depositions.

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MR. NIGH: The other -- you mean the other depositions using Veritext? Because I don't think that we need to be breaking to switch tapes. This is being done via Zoom, and it's being recorded via Zoom. I just don't understand why we would -- why we would break unnecessarily.
MR. GALLAGHER: Let me finish up for 10 minutes, and then we can talk about that.
BY MR. GALLAGHER:
Q So looking under "Exposure Assessments" --
A Okay.
Q -- we had looked at this earlier, that the -- the measurements of NDMA are based on estimates from a database. And then further on, about halfway through this paragraph, it says, "Because only job information in 1967 was available, the primary analyses assumed all subjects remained in the same factory department, i.e., not necessarily in the same job, throughout their careers and were employed until retirement at age 70, death or immigration."
Do you see that?
A Yeah.

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Q So in addition to NDMA not actually being measured but being based on estimates from primarily German factories, in Hidajat, in this cohort, they didn't know what part of the factory these individuals were actually working in. They only had job information for one year, and they assumed that they stayed in the same department, right?
A Can I just have a few minutes to read this, if you don't mind?
Q Sure.
A I'm actually going to look at Hidajat at the very end in the discussion.
Q Sure, what --
A What was the exhibit number again for Hidajat?
Q Exhibit 8.
A Okay. Just one second, please.
Q Sure.
A Okay. So would you please repeat your question?
Q Sure.
So in addition to not actually measuring NDMA but relying on estimates that came primarily from measurements of German rubber

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factories, because job information was only available for one year, 1967, the authors assumed that all the subjects stayed in the same factory department throughout their career. But they don't know if any of these workers moved -- moved around to various different departments?
A So, I mean, obviously, it's challenging to keep track of people -- people's occupation for 35 years. However, I think they took this issue seriously, and they do mention that they did sensitivity analyses looking at different duration of employment. And they mentioned that that didn't change the results.
Q So I understand that they did some sensitivity analyses around duration of employment, but they're still assuming that for the duration of employment, each subject is staying in the same factory department, right?
A Yeah. There is that assumption, but at least, you know, the sensitivity analysis of the different duration of employment, I believe is reassuring. But, yes, the assumption is that they did stay in that -- in that employment for -- for the amount of time.
Q So the sensitivity -- sensitivity

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analysis around duration of employment, I understand that addresses the duration of employment, but that doesn't address this assumption that all the subjects are staying in the same department.
MR. NIGH: Form objection.
THE WITNESS: I mean, I'm not sure, honestly, whether different departments would have different exposure to NDMA over a 35-year period. But that -- that's -- I mean, that's just the nature of the study. And that's what they mention. Again, it -- the exposure of NDMA in the different departments for it to change a major cause and major bias in the study, it has to be quite big and only affecting one group as -- as we talked about with other types of carcinogens, to maintain -- to change the direction of these results.
BY MR. GALLAGHER:
Q So if we go back to the first page of Hidajat, the right-hand column, bottom paragraph, the authors expressly say, "Exposures vary throughout the rubber manufacturing process."
A Exposures do vary, but my -- I think my point was exposure has to vary in one group, the high NDMA, for -- constantly for long periods, and

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they don't have to -- and they shouldn't vary or stay static in the control group for a long period for this -- for this bias to be introduced. If exposure -- varied exposure happens randomly through the population of these men in 35 years, again, that could maybe affect the precision a little bit then. But it shouldn't change the direction of the -- of the risk.
Q But you're assuming the exposure to NDMA. And what the -- the authors are admitting on Page 251 is they only have job information for one year. So they're assuming that all subjects stayed in the same department. They don't -- they don't know if they moved.
MR. NIGH: Form objection.
BY MR. GALLAGHER:
Q Right?
MR. NIGH: Form objection.
THE WITNESS: They don't know if they moved, yeah.
BY MR. GALLAGHER:
Q Okay. And then additionally, if we go forward to Page 257, the right-hand column, the paragraph just above "Conclusions." So in this paragraph, Hidajat is acknowledging several

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limitations of -- of the study, right?
A Uh-huh.
Q Including the final sentence, "Finally, cross-contamination between departments cannot rule out the need for multi-pollutant models," right?
A Yeah.
Q "But given the high correlations between exposures, this requires different and complex statistical modeling with currently unknown validity in this context," right?
MR. NIGH: Form objection.
THE WITNESS: Right. Again, I go back to my -- the point that I have been repeating, the cross-contamination, for it to change the direction of the results, has to be differential only in one group. And I think they are just -- they are just listing one of the limitations that the study in general. But for this cross-contamination to change the consistent -- the increased risk of cancer in this study, it has to be a major differential factor. And I -- I believe that if it was, the authors would mention that in their limitations as well. Rather than just, you know,

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mentioning that there could be cross-contamination, they would maybe elaborate that the cross-contamination has affected these results because -- and they don't say that. And I don't have any reason to believe there was a major differential contamination in one group versus the other group.
BY MR. GALLAGHER:
Q So -- but, again, this is impacting the actual measurement, so if we go back to the first page again, that paragraph we were just looking at, that says, "Exposures varied throughout the rubber manufacturing process." And then they go on to say, "Rubber dust tends to have the highest exposure in the beginning of the production process, particularly in handling of raw materials," right?
A Right.
Q And then, "Rubber fumes and N-nitrosamines are generated during the heating and curing processes," right?
A Right.
Q So Hidajat is basing their exposure to NDMA on the estimates of exposures in the various -- in the various parts of the factory, right?
A Right.

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MR. NIGH: Form objection.
BY MR. GALLAGHER:
Q They're not -- they're not actually measuring what the exposure to NDMA is, right?
A Well, I mean, I don't think that's -- that's very, very difficult to do, so they are using the estimates. I think we have talked about this already.
Q Sure. And the limitation that they're acknowledging is potential for cross-contamination between departments. So if there was contamination of rubber dust into the department that was doing the heating and curing processes, that would have a huge impact on the assumption that the people in the heating and curing processes are the ones most highly exposed to N-nitrosamines and basing their conclusions of the hazard ratios off of that, right?
MR. NIGH: Form objection.
THE WITNESS: Again, that cross-contamination has to be sustained for duration of the followup and only in the NDMA -- high NDMA category, to cause the type of bias that you're talking about.
BY MR. GALLAGHER:
Q So that's what I'm saying, is the

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cross-contamination would, because the high ND -- they're classifying people in the cohort as either high NDMA or low NDMA based on where they're working in the -- in the factory; is that right?
MR. NIGH: Form objection.
BY MR. GALLAGHER:
Q In other words, that's their assumption. If there's actually cross-contamination into that department of, for example, rubber dust, just to use one, then their -- their assumptions -- or their assignment of those individuals being high NDMA, it is directly impacting 100 percent of those people, differentially?
MR. NIGH: Form objection, argumentative.
THE WITNESS: Yeah. I don't -- I'm not sure if I agree with that. I mean, that's -- that's -- I think that's quite a stretch of what -- what could have happened. There is no -- I mean, I think you're just -- I mean, you're -- you're coming up with an assumption. But I don't -- I mean, even in this -- the limitations of their study, they don't mention such a huge limitation as a potential reason for the results that they found.

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THE VIDEOGRAPHER: Counsel, there's about three minutes remaining.
MR. GALLAGHER: Okay. Why don't we go ahead and take a break?
MR. NIGH: I'm sorry. Are we taking a break because there's three minutes remaining on tape? Because we're -- we're ready to keep going. I mean, if this is going to be 10 hours of record time to have interruptions just because there's a certain amount of record, you know, tape time, this is not an interruption that we've had for any other court reporter. And I don't understand why we would have it here.
We have not had this for any of our depositions that the plaintiffs have taken of custodial depositions. And frankly, I think that this is not a reason to take a break. I want to us continue forward at this time.
Dr. Etminan, can you continue? Do you want to continue forward?
MR. GALLAGHER: Let's take a break.
MR. NIGH: No. No. No. We don't just take a break because -- because there's a limitation for -- for tapes for some reason

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that we can't even get an explanation for.
MR. GALLAGHER: Can we go off the record and discuss that?
MR. NIGH: No. No. I want this on the record because I want to be arguing that if we're going to have 10 hours of record time, that we need to be getting through the deposition, not taking breaks just because there's a limitation in terms of tape time. This should not be -- this should not be a limitation for a Zoom deposition. We're ready to continue forward.
THE VIDEOGRAPHER: Counsel, there's one minute.
THE COURT REPORTER: Your court reporter needs a break.
MR. NIGH: This is all coming out now in response to the tapes. I can tell. So you know we -- we need to be getting through this deposition, and now -- now, we're -- it is -- this prompt was clearly because of tapes. That's what I heard. That's what started the whole thing. Now, it's sounding to me like other people are weighing in to try to save this response on the tapes. This happened

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multiple times in other depositions, and that's exactly what I think the record is going to show here as well. We can go ahead and take a break.
THE VIDEOGRAPHER: The time is now 1:57. This is the end of Media Number 2. We're going off the record.
(Whereupon, a short break was taken.)
THE VIDEOGRAPHER: The time is now 11:13. This begins Media Unit Number 3. We're back on the record.
BY MR. GALLAGHER:
Q Okay. Dr. Etminan, looking at the Hidajat article again, Exhibit 8, it's the sentence starting on the first page, very bottom of the first page. It's only two words, "Due to," and then moving on to the beginning of the second page, Page 251, the author states, "Due to the complexity of exposure pattern and the numerous chemicals used in the rubber production process, this entangling exposure response associations between specific suspected carcinogens and cancer risks in this industry remains difficult."
Do you see that?
A Yes.

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Q And so the authors are acknowledging that while working in the rubber industry may be a significant risk of cancer, using occupational studies of the rubber industry to evaluate exposure response associations for a specific suspected carcinogen is something that's difficult to do, right?
MR. NIGH: Form objection.
THE WITNESS: Yes. That's what they say. But I think that part of -- part of what they're saying is to kind of strengthen their case as to why they did this study. I mean, this is in their introduction. But I mean, as a general statement, I -- I agree with -- with what is said.
BY MR. GALLAGHER:
Q Okay.
MR. GALLAGHER: If we can move on now to the next exhibit, are we at 10, Exhibit 10, the Lavecchia article?
THE COURT REPORTER: Can you spell that?
MR. GALLAGHER: Sure. Lavecchia, L-a-v-e-c-c-h-i-a.
THE COURT REPORTER: Thank you.

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(Whereupon, Exhibit 10 was marked for Identification.)
THE WITNESS: I have it.
BY MR. GALLAGHER:
Q Okay. You relied on this study for your opinions related to gastric cancer; is that right?
A Yes. This is just the abstract, though. It's not the full PDF.
Q Right. Let me correct that.
MR. GALLAGHER: Okay. Can we go off the record for just one minute.
THE VIDEOGRAPHER: Sure. The time is now 11:17. We're going off the record.
(Whereupon, a discussion was held off the record.)
(Whereupon, Exhibit 11 was marked for Identification.)
THE VIDEOGRAPHER: The time is now 11:19. We're back on the record.
BY MR. GALLAGHER:
Q Dr. Etminan --
MR. NIGH: Hold on. Before you ask -- ask a question, I want to put on the record that we just had to take a three-minute break

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to go off the record so that Counsel could substitute the "Nitrosamine Intake and Gastric Cancer Risk" abstract for the full study.
Do you disagree that's the reason we just went off the record, Mr. Gallagher?
MR. GALLAGHER: I don't understand your -- your -- all your troubles about taking breaks. I've never been in a deposition where we didn't take breaks for the court reporter, for the witness, for everybody, so --
MR. NIGH: I have been in many depositions where --
MR. GALLAGHER: -- we can take a break --
MR. NIGH: I have been in many depositions where we've -- especially expert depositions, where we have been able to go two hours at a time, and where the expert is at-will to be able to take the breaks.
At this point, the expert has not asked for a single one of these breaks that we've had at this point. And so, yes, I am concerned about excessive breaks when we have 10 hours of record time. That leads to many hours of not record time.

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MR. GALLAGHER: But --
MR. NIGH: No. You asked why I'm concerned. I am concerned. So here we just had another break that was not anything asked for by the witness. It was yet again you, Mr. Gallagher, here that just had the wrong document. All I wanted to do was put the reason for the break on the record. I asked if it was true. Do you agree that that was the reason for the break?
BY MR. GALLAGHER:
Q Dr. Etminan, do you have in front of you Exhibit 11?
A Yes.
Q And this is the Lavecchia article?
A Yes.
Q And you relied on this study in relation to your opinions related to NDMA and gastric cancer in this case, right?
A Right.
Q If you look at the abstract on the first page, the last sentence, you will see it says, "Limitations of exposure assessment and absence of information on other N-nitrosamines preclude, however, any definite assessment of the possible

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role of exogenous N-nitrosamines in gastric carcinogenesis."
Do you see that?
A Yes.
Q And so the -- the authors are acknowledging that they can't make any definitive assessment of an association between exogenous N-nitrosamines and stomach cancer because of that limitation, right?
MR. NIGH: Form objection.
THE WITNESS: That's -- that's what they're suggesting, yes.
BY MR. GALLAGHER:
Q Okay. And they refer here to specifically exogenous N-nitrosamines, right?
A Yes.
Q Do you have an understanding of the distinction between endogenous NDMA and exogenous NDMA?
A To -- to -- you know, to certain levels, yes.
Q Okay. You haven't addressed anywhere in your report the -- the -- any potential impact of endogenous NDMA, have you?
MR. NIGH: Form objection.

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THE WITNESS: No, because it's -- it's very difficult to quantify and ascertain endogenous NDMA exposure. I'm not familiar with any sort of robust gold standard, if you will, method to do it, because it's so complex. But then again back to what we discussed before, endogenous NDMA, you have to have a good reason why one group -- endogenous NDMA can be -- we can all be exposed to endogenous NDMA. It's a very complex sort of process to quantify.

But then, again, how can we actually say that one group in this study is exposed to more endogenous NDMA than the other? And that's -- and why -- and there's no reason to believe that's the case. So that's -- that's why I didn't discuss it in my report.

BY MR. GALLAGHER:

Q Okay. Why don't we turn to Page 472 of this article?

So, Dr. Etminan, you say that there's a lot of complex factors that can influence endogenous NDMA; is that right?

A Yes.

Q Okay. And that's why you didn't

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include it in your report or address it because it was complex?

A I mean, again, it's very hard to quantify and discuss it in most of the studies that I looked at it, and there's a lot of them. It wasn't really mentioned or measured, so for the whole host of reasons, that's why I mainly focus on exogenous NDMA.

MR. NIGH: And I object to the form of the last question.

BY MR. GALLAGHER:

Q Looking at the left-hand column here on Page 472, the sentence right above the last paragraph starting with, "However," the authors say, "However, we had no information on endogenous N-nitroso compound formation, which is influenced by gastric PH levels and other complex factors including microbial species in the mouth and stomach, N-nitrosation inhibitors besides subjective individual variation."

Do you see that?

A Yes.

Q So the -- the authors of the Lavecchia study acknowledge the potential issues with not having information on endogenous N-nitroso compound

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formation influenced by all these complex factors, right?

A I mean, they say that -- yeah, I mean, they say that's something that they probably won't -- would have liked to have had and address. But they don't go as far as saying that they think the results of their study could have been changed because of endogenous NDMA exposure.

And, again, I think it's because there is no reason to believe that the controls in the cases vary very differently coming from the same sort of population in terms of endogenous NDMA exposure.

Q But, again, unless you actually evaluate that, you don't know if there's a differential effect of --

A Yes -- for certain. Like, if you want to be certain whether there is a change in the effects, yes, you have to evaluate. But I am -- again, I don't really know -- as far as I know, there are no sort of gold standard measurement tools to measure this in -- and incorporate it in an epi study.

THE COURT REPORTER: In a what study?

THE WITNESS: In an epidemiological

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study.

MR. GALLAGHER: Can we mark as Exhibit 12 an article by Jakszyn, J-a-k-s-z-y-n, from 2006.

And, Doctor, let me know when it shows up and you have it.

THE WITNESS: Oh, sure. Sure.

(Whereupon, Exhibit 12 was marked for Identification.)

THE WITNESS: Okay. I got it.

BY MR. GALLAGHER:

Q You got it? Okay.

So the title of this article by Jakszyn is "Endogenous versus exogenous exposure to N-nitroso compounds and gastric cancer risk in the European Prospective Investigation into Cancer and Nutrition Study." Is that right?

A Yes.

Q So in this study, they did try to evaluate -- to measure and evaluate the potential impact of endogenous N-nitroso compounds, right?

A Yeah, seems like it.

Q Okay. And looking at the abstract, on the right-hand column -- of the top of the right-hand column of the first page, in this study,

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they also were evaluating potential association of NDMA intake with risk of gastric cancer, right?
A Yes.
Q And you see about halfway down they say, "There was no association between NDMA intake and gastric cancer risk," right?
A Sorry. Where are you referring to?
Oh. Yes, that's what they say.
Q Okay. And their observed hazard ratio for any potential association of NDMA intake and gastric cancer risk was exactly 1.00, right?
A Right.
Q And we had talked about a hazard ratio of 1 means there's no evidence of an association between the exposure and the risk, right?
A Right.
Q So in this study, when they were -- they also evaluated endogenous N-nitroso compounds. That's abbreviated ENOC, right?
A Yes.
Q And there in the abstract they concluded -- or their data for endogenous N-nitroso compounds, the ENOC, was significantly associated with non-cardia cancer risk, right?
A Yes.

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Q If we turn to Table 1, which is on Page 1499.
A Uh-huh.
Q And this is providing a description of the sample included in the cohort. And do you see it's providing mean values for certain of the -- of the variables, including NDMA and endogenous N-nitroso compounds?
A Yeah.
Q The mean endogenous N-nitroso compounds in the -- in the study was 93.05 micrograms per day, right?
MR. NIGH: Object to form.
THE WITNESS: How many --
BY MR. GALLAGHER:
Q And that would be 93,050 nanograms per day; is that right?
A Micrograms per nanograms.
THE COURT REPORTER: I'm sorry. Can you repeat that?
THE WITNESS: I was just saying micrograms per nanograms.
Can I just have a few minutes to read this, if you don't mind?

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BY MR. GALLAGHER:
Q Sure, sure.
MR. GALLAGHER: So, Daniel, in our depositions when the witness needed a long time to review a document, we went off the record. My question is pretty simple.
MR. NIGH: We can go off the record.
MR. GALLAGHER: Okay. Off the record.
THE VIDEOGRAPHER: The time is now 11:38. We're going off the record.
(Whereupon, a short break was taken.)
THE VIDEOGRAPHER: The time is now 11:38. We're back on the record.
MR. GALLAGHER: Thank you. And can the court reporter read back the last question.
(Whereupon, the testimony was read back as requested.)
BY MR. GALLAGHER:
Q Dr. Etminan --
A Yes. So with respect to the lack of -- risk with exogenous NDMA, I think I have addressed this in my report at the follow-up of the study. It was only about 3 and a half years, which is inadequate for an exogenous carcinogen causing cancer, and also, I do mention that just from the

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demographics of the study, which are mainly --
THE COURT REPORTER: Which are mainly what?
THE WITNESS: Elderly, older adults.
That they may have died before getting cancer, which usually has a longer sort of an onset. With respect to the 93,000 exogenous values, I -- the value seems quite high to me. And I don't -- I'm not familiar with the methodology that they used. And, again, I'm not saying that it's not the right methodology, but I just haven't seen any other study measuring endogenous NDMA as well.
BY MR. GALLAGHER:
Q Okay. In this study where they address endogenous and N-nitroso compounds, the mean endogenous N-nitroso compound in the -- in the study was 93,050 nanograms per day, right?
A Yes.
Q And if we go back to the abstract --
A Yeah.
Q -- the -- after presenting the hazard ratios for endogenous N-nitroso compounds, they go on to say, "Although the number of not infected cases is low, our data suggests a possible

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interaction between ENOC and H. pylori infection," right?
A Yes.
Q So they're seeing a possible interaction between an impact of endogenous N-nitroso compounds and infection with H. pylori?
MR. NIGH: Form objection.
BY MR. GALLAGHER:
Q Right?
A Yeah, the interaction basically means that the levels of the -- the risk of cancer with endogenous NDMA changes with levels of H. pylori, so I mean, they have H. pylori measured. So that's what they found. That's -- I mean, I agree with that.
Q Right. And so in this study where the authors accounted for endogenous N-nitroso compound and accounted for H. pylori infection, with respect to NDMA, the data showed no association between NDMA intake and gastric cancer, right?
A You mean --
THE COURT REPORTER: I'm sorry. You mean what?
THE WITNESS: No association with exogenous NDMA?

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BY MR. GALLAGHER:
Q Yes, no association of exogenous NDMA intake and gastric cancer risk?
A Right. But I think I did address that, although those are restraints of the study, the limitation -- I mean, not showing an association is also dependent on other factors. One, you need an adequate follow up to be able to detect the cancer. Two, you need to control for deaths other than cancer, which may sort of lower the -- your sample size. So you have to address for that, which they haven't.
So I can't -- because they have other limitation -- methodological limitations, I can't just say, you know, there is no risk because they control for H. pylori and endogenous NDMA. There are other issues in the study design.
Q So with respect to the -- the time for follow up, it was sufficiently long since they identified a significant association of endogenous N-nitroso compound with non-cardia cancers, right?
MR. NIGH: Object to form.
THE WITNESS: Right. But I mean, the mechanism of cancer with exogenous, I mean, could take longer. And so you need to -- you

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may need a longer follow up for that to be picked up.
THE COURT REPORTER: Could be what?
THE WITNESS: You may need longer follow up for the exogenous for -- for cancers from exogenous NDMA to be picked up or to be detected.
THE COURT REPORTER: Thank you.
BY MR. GALLAGHER:
Q Why do you -- why do think it would take longer for an exogenous?
A Because you have to be taking it constantly, and it has to be ingested and then absorbed systemically. And it's possible that the mechanism of carcinogenesis with exogenous NDMA may -- may be different.
Just like when you have a drug that's culled in your system, it's -- it's getting absorbed more than if you're taking a pill every day that's only 20 percent absorbed. So the -- the constant exposure and the concentrations may be different.
MR. NIGH: Object to the form of the last question.
BY MR. GALLAGHER:
Q So you're telling me that the time

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frame of exposure to an -- to an exogenous carcinogen --
A I'm just saying that should -- it's possible that the -- sorry. I should have let you finish.
I'm just saying that the follow-up time for the exogenous NDMA to show cancer events where they could actually pick it up would have been -- could have been higher -- you know, longer than just the 3-year or 3-and-a-half-year follow up that they had.
Q And am I understanding right that you're saying the reason for that is because the time frame of exposure to an exogenous carcinogen is --
A Well, I mean, you don't --
THE COURT REPORTER: I'm sorry -- I'm sorry, Doctor. I'm not hearing the -- I'm not hearing the end of the questions, and therefore, I'm not having the full question on the record. If you could just take a deep breath and let Patrick finish his question before answering, I would appreciate it.
THE WITNESS: Okay.
MR. GALLAGHER: My apologies to the

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court reporter and to Dr. Etminan.
BY MR. GALLAGHER:
Q So am I understanding properly, you're saying that the reason for that is because the time frame of exposure to an exogenous carcinogen is a significant factor in the potential for actual risk of cancer?
MR. NIGH: Object to the form.
THE WITNESS: Perhaps I would call it induction time, which means the time from being exposed from exogenous NDMA, which may take longer to the cancer process to occur and be diagnosed. Whereas, the endogenous, it's already in the system. Whereas, the exogenous, you need to be exposed to it, you know, constantly through -- orally or through the skin or through inhalation. So it may take longer for the NDMA to cause its carcinogenic effect for the cancer process.
BY MR. GALLAGHER:
Q Okay. You mentioned a few minutes ago and also in your report one aspect of -- of this study that you considered to be a material limitation is that it included in mostly older adults? Do I understand that right? And if you

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want to look at Page 17 of your report, if you want to look at it is where you're discussing this.
A Yes.
Q Okay. So you recall that it's one of your criticisms of this -- of this article, right?
A Right.
Q If we look on Page 1498 of the article, just under "Material and Methods for Subjects," this cohort included women and men aged 35 to 70 years, right? So their age range is 35 to 70, right?
A Uh-huh.
Q And if we look at table 1, the mean age at recruitment was 59.2, right?
A Right. So -- sorry. Can I address --
Q Yes.
A Yes. So 60 is a year where, you know, they have cardiovascular disease. You could have diabetes. It's the year where these conditions these are prevalent. And deaths due to these conditions, the risk for -- for deaths due to diabetes and cardiovascular disease and other co-morbid condition is -- is also increasing.
So if patients die for these causes and not live -- live long enough to get cancer, that

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is a bias that should be addressed, should have been addressed in this study. That's what I was referring to.
Q And then additionally, the -- so let me ask you this: Those other co-morbid conditions are factors from your perspective to be considered because they can impact -- could have impacted the results of this study?
A As you can see in Table 1, there's no -- there's no information given on -- as they have with the other variables, on the percentage and -- and the breakdown of other co-morbid conditions. I mean, if -- if the cases we're sicker, get more ill, because of these kind of conditions, could that have affected, you know dying of -- of cancer, including the ones that were -- that died because of endogenous exposure. So I think that those are potential confounders that should have been adjusted for. And they were not. They were only adjusted for things like smoking and diet and physical activity, which are important, but there are other potential confounders which I think should have at least been mentioned as to why they --
THE COURT REPORTER: As to why they

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were what?
THE WITNESS: They were not controlled for.
BY MR. GALLAGHER:
Q Do you know what the age of the cohort was for the --
THE COURT REPORTER: For the what study?
MR. GALLAGHER: Hidajat.
THE WITNESS: I can look -- look it up right now. I don't know off the top of my head.
BY MR. GALLAGHER:
Q Okay. So if we go to Exhibit 8, Page 251.
A Uh-huh.
Q Under "Material and Methods," the data is from male UK rubber factory workers aged 35 years or older as of 1 February 1967, right?
A Right.
Q And it's not -- perhaps not that surprising that in a cohort study, looking at risks of cancer, the cohort is including older individuals, right?
A Right. But -- but what Hidajat did

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unlike -- none of the other studies that I have seen, is, if you look at Page 251 under "Statistical Methods," they did a special modeling technique called "Fine and Gray," which controls for death because it was such a long study with such a long follow up of say -- in 35 years. So people started at 35, but they would get to 50 and 60 and, you know -- in 10, 20 years, which is -- puts them at risk of other deaths, which as we've talked about, can bias the results if it's not -- if they're not accounted for. If they drop out of deaths other than cancer, then they don't get to get cancer. So they actually controlled for that with the Fine and Gray analysis.

Q And as people get older, one of the -- one of the risks for getting cancer is getting older, right?

A Right.

Q Okay. You also criticize the Jakszyn study for not controlling for confounders such as history of stomach cancer, right?

A Yes.

Q If you look on Page 17 of your report --

A Right.

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Q -- that was one of your criticisms of the Jakszyn study.

A Uh-huh.

Q So the Hidajat study didn't control for confounders like history of stomach cancer, right?

A You're right. They did not. But again, just the sheer size of the -- the sample size, the very long follow up, that -- that confounding factor, which theoretically is a confounder has to be disproportionately, you know, higher in the high NDMA group than the low NDMA group. And given this is a population-based study where to some accounts the rates are, you know, probably stable over time, or go up, you know, a little bit just like most European countries in the UK, I don't see why absence of that confounder would have made any difference. Whereas here with Jakszyn, it's a much smaller study, only a 3-and-a-half-year follow up. So I'm -- and I believe it's -- I'm just looking at the sample size. I believe it's a smaller sample size --

THE COURT REPORTER: I'm sorry. Than what?

THE WITNESS: Than Hidajat. No. It's

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a bigger study. It's a bigger study. It's a bigger study. But I believe it's got smaller number of cases than Hidajat does, because Hidajat followed for a long time. So there are more cases.

BY MR. GALLAGHER:

Q Okay. So you agree with me that the -- the Jakszyn study, which evaluated exogenous NDMA intake as well as endogenous N-nitroso compounds is a larger study than the Hidajat study?

A Number-wise, yes. Number-wise, it is.

MR. NIGH: Object to form.

BY MR. GALLAGHER:

Q And you criticized the Jakszyn study for not controlling for confounders like history of stomach cancer, right?

A Yes.

Q And the -- the Hidajat study also didn't control for confounders like history of stomach cancer, right?

A Yes.

Q And so that same criticism applies --

A It does.

THE COURT REPORTER: I'm sorry. Can you repeat that?

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BY MR. GALLAGHER:

Q That same criticism of not controlling for confounders like a history of stomach cancer would be a criticism of any study that didn't account for that confounder?

A That's right. But keep in mind that I -- I sort of came up with my opinion on stomach cancer, not just on Hidajat alone and Jakszyn alone. It was the totality of evidence. And there are --

THE COURT REPORTER: I'm sorry. I'm sorry. What was that?

THE WITNESS: Lavecchia, the study we just talked about before this one, did control for stomach cancer history.

BY MR. GALLAGHER:

Q Okay. What does that mean to you -- I understand you didn't base your opinions solely on the Hidajat and the Jakszyn study. What does that mean to you, though, to be looking at the "totality of the evidence"?

A Totality of the evidence means biologically plausible evidence, which is mostly from animal studies; data from, mainly, Hidajat; from occupational studies; and data from dietary studies. And, again, it doesn't mean that every

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single study is a perfect study that shows an increase in risk, and they don't have limitations. But the constellation of all of the evidence is what I weighted my opinion on.

Q Okay.

MR. GALLAGHER: Can we mark as the next exhibit, Exhibit 13, the Palli study.

(Whereupon, Exhibit 13 was marked for Identification.)

THE COURT REPORTER: Can you spell that?

MR. GALLAGHER: P-a-l-l-i.

THE COURT REPORTER: Thank you.

BY MR. GALLAGHER:

Q And, Dr. Etminan, you discuss this study at the top of Page 17 of your report.

A Okay.

Q Dr. Etminan, in this study, there was --

A Sorry. Sorry. Just give me one second to read this paper.

Q Sure.

A Okay. Go ahead.

Q This study did not find a statistically significant association between NDMA

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and the risk of gastric cancer, right?

A It found an odd ratio of two that just missed statistical significance.

Q But it did miss statistical significance, right?

A Yes.

Q This study also reported a statistically significant increased risk for gastric cancer based on family history, right?

A Yes.

Q And family history for gastric cancer would be a known risk factor, right?

A It would be.

Is there a table that I should refer to or any numbers here?

Q Sure. You can look at -- we can look on Page 165.

A Sorry. Palli is Pages 1206 to --

Q Oh, sorry. It's the third page of the PDF, Page 165. There's Table 1.

A Okay.

Q Showing the family history and then in the left-hand column under "Results"?

A Uh-huh.

MR. NIGH: Are you following along on

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Page 165 because I don't see a 165?

THE WITNESS: It's Page 1208.

MR. GALLAGHER: I think we need a different --

MS. APPEL: Yeah, I'm sorry --

MR. GALLAGHER: No worries.

MS. APPEL: (inaudible)

BY MR. GALLAGHER:

Q So we'll get there. But, Dr. Etminan, let's talk just -- let's talk about family history of gastric cancer.

Do you acknowledge that that is a known risk factor for a person to develop gastric cancer if they have a family history of gastric cancer, right?

A Yes.

Q And the -- the Hidajat study and the Lavecchia study, they didn't account for that?

A Yes.

Q -- as a factor -- as a factor, right?

A No.

MR. GALLAGHER: So Exhibit 14 should be coming. It's a Palli study.

(Whereupon, Exhibit 14 was marked for Identification.)

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THE WITNESS: Okay.

BY MR. GALLAGHER:

Q Dr. Etminan, have you seen this article before?

A It's by Palli, so I may have seen it, but included the one that I -- included within my report, because it's pretty much from the same authors.

Q So can you explain that to me again? Have you seen this before or not?

A I may have, but I haven't included it in my report. I may have seen it in my search.

Q Okay. So you're not relying on this -- can you turn to your report, which is Exhibit 5, I think?

A Sorry.

Q Turn to your report, Exhibit 5, and on Page 17...

A Yes.

Q And you see at the top of Page 17, you refer to a population-based case controlled study conducted by Palli, right --

A Yes.

Q -- in Citation 43?

A Yes.

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Q Can we go to Page 38 of your report?
A Yes.
Q And so the citation for 43 is to Palli, an article titled "Dietary Patterns, Nutrient Intake and Gastric Cancer in a High-Risk Area of Italy," right?
A Right.
Q And that citation is to the article that we were just looking at that's Exhibit 14, right?
A Right.
Q But you said you didn't rely on this for your report?
A Right. I thought there were two Palli studies that you showed me. The one Palli study that I cite in my report, I believe, is this one. Yes. It's this one because it's 382 gastric cancer cases, and that's what I have. So it's this one.
Q Okay.
A By Palli, Russo and Decarli.
Q I think we're confused because the article that you -- the Palli article you produced to us was the other one.
A Okay. Sorry.
Q Okay. Okay. So if we -- if we look

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at Exhibit 14, on Page 165, the third page of the PDF, Table 1, it's presenting the data with respect to family history.
A Yes.
Q And in the description of the results, which is starting on the left-hand column of this same page, the authors state, "A positive family history for gastric cancer among parents or siblings, rural residence and lower social class were strongly associated with increased risk"?
A Yes.
Q So all of those -- the Palli study was able to determine that all of those factors were strongly associated with risk of gastric cancer, right?
A Those are risk factors, yes.
Q Okay. But there was no -- no statistically significant association between exogenous NDMA intake and gastric cancer from this study, right?
A No.
MR. GALLAGHER: Can we mark as Exhibit 15 the Loh paper, L-o-h.
(Whereupon, Exhibit 15 was marked for Identification.)

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MR. GALLAGHER: Actually, I'll come back to that one. Can we mark the Kefzei paper and this will be Exhibit 16. K-e-f-z-e-i.
THE COURT REPORTER: K-e-f-z-e-i?
MR. GALLAGHER: Correct.
(Whereupon, Exhibit 16 was marked for Identification.)
THE WITNESS: I have it open.
BY MR. GALLAGHER:
Q Okay. And this is a paper that you refer to also on Page 17 of your report, right?
A Yes.
Q So the -- if we pull up Page 17 of your report that would be helpful.
A Yeah.
Q The paragraph on Kefzei, "The adjusted --" "The adjusted risk of gastric cancer" --
A I'm sorry. So -- I'm sorry. You're not on Loh then? You want to look at Kefzei?
Q Sorry. Yes.
A Okay. Let me get that. Let me get that. Okay.
Q So you say that, "The adjusted risk of gastric cancers with nitrosamine intake among men

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was elevated by 6 percent, and you're basing that off of a hazard ratio of 1.06," right?
MR. NIGH: Objection.
BY MR. GALLAGHER:
Q And that's for one type of gastric cancer, right?
A Yes.
Q And then you acknowledge that this is not for other types of gastric cancer, gastric cardia, although the observed hazard ratio is 1.31, that did not --
THE COURT REPORTER: I'm sorry. That's not very specific...
THE WITNESS: It did not reach statistical significance.
BY MR. GALLAGHER:
Q Did not reach statistical significance.
A Yeah.
Q You see that, right?
A Yes.
Q And then among women, the risk was also not elevated, right?
A Correct.
Q And you go on to say, "The lack of an

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effect in this study," so you acknowledge that in this study, there's a lack of any association of exogenous NDMA with gastric cancer, right?
MR. NIGH: Object to form.
THE WITNESS: That's -- yes.
BY MR. GALLAGHER:
Q Okay. And you go on to try and -- one issue that you raised is a potential for misclassification of the diet questionnaire used in the study?
A Yes.
Q Right? That potential for misclassification that you're referring to is potential inaccurate reporting of -- of food intake by the subjects in the study, right?
A Correct.
Q Okay. Isn't that true of every dietary study that's based on a diet questionnaire?
A Yes, it could -- it could occur in any dietary study.
Q So the -- I guess what I want -- so regardless of whether the observed association is showing no association or showing some association, there is -- this is a criticism of dietary studies generally, the potential for inaccurate reporting

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of -- of food intake, right?
A That's the one limitation of all dietary studies, right.
Q Okay. So -- let's move on then.
MR. GALLAGHER: Can we mark the Song study as -- are we at -- what exhibit number are we at?
(Whereupon, Exhibit 17 was marked for Identification.)
MR. GALLAGHER: So this will be Exhibit 17, the Song article.
BY MR. GALLAGHER:
Q Let me know when you have it, Dr. Etminan.
A I have it now.
Q Okay. So you agree with me that this is -- this article is reporting on a meta-analysis?
A That's correct.
Q Okay. Have you conducted a meta-analysis before?
A Yes.
Q Okay. And this is a meta-analysis of observational studies, right?
A Yes.
Q Is one of the limitations of a

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meta-analysis observational studies the potential for confounding variable?
A I mean -- yeah. I mean, that's a limitation of observational studies as well, yes.
Q So for any meta-analysis of observational studies, you would agree that residual confounding factors may distort the results?
A I mean, there is a potential, theoretically, yes.
Q So have you actually seen this article or just the abstract for it?
A No. I have seen -- I have -- I mean, I have looked at the numbers and the tables as well.
Q Okay. So if we look on -- do we have Page 9892?
A Okay.
Q So I guess, I think I asked this question somewhat generally although it applies to the -- certainly to the Song meta-analysis.
You would agree with me that measurement errors resulting from dietary questionnaires can impact the reliability of dietary studies, right?
MR. NIGH: Form objection.
THE WITNESS: Generally speaking, I

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think we've -- we've talked about this, yes.
BY MR. GALLAGHER:
Q Okay. And dietary questionnaires -- a questionnaire doesn't ask subjects, how much NDMA did you eat -- the dietary, right?
A Yes. They ask about the dietary patterns of individuals, and then they convert the food groups to -- they convert the NDMA content in each food group based on the information they have on the amount of NDMA in each food category.
Q Okay. So it may ask, how much bacon do you eat, how much fish, how much fruit?
A That's right.
Q And then -- and then from there, the authors or the people conducting the study estimate NDMA intake for the subjects based on estimates for the amount of NDMA or any other compound in that particular food group, right?
A That's right.
Q And if those -- if those estimates are wrong, that also impacts the validity of the results from a dietary study?
A Also, I mean, potentially. We have talked about this. It's a limitation of dietary study.

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Q Okay. Let's go back to your report. We'll look at Page 18 and Section 10.2 at the bottom of the page.
A Okay.
Q It's is referring to colorectal cancer.
A Okay.
Q So for colorectal cancer, Hidajat didn't look at colorectal cancer right?
A No.
Q Didn't examine -- okay.
And the Straif occupational study did not find any specifically significant association, right?
A No.
Q Okay.
A Because I think it was just they didn't have enough cases because they -- I don't think they had enough number of events. But the answer to your question, is no.
They found a relative risk of one-and-a half, but because of the small number of events, it was very imprecise and not statistically significant.
Q What was imprecise?

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A The confidence interval. It was from .5 to 4.7, around the 1.5 estimate.
Q Right. And so because the confidence interval includes 1.0, there's -- there's no evidence of an association, right?
A No, I -- again, I think I talked about this earlier. It's -- the relative risk is 1.5 based on very small number of events. And that 1.5 comes with a very imprecise estimate. We cannot necessarily say that there is no increased risk. We can say that it's imprecise, and the results are basically -- I'm trying to find the right word. Uncertain, if you will.
Q Okay.
MR. GALLAGHER: Can we mark the Knekt paper? This will be Exhibit 18, I believe.
(Whereupon, Exhibit 18 was marked for Identification.)
THE COURT REPORTER: How do you spell that.
MR. GALLAGHER: K-n-e-k-t.
BY MR. GALLAGHER:
Q Let me know when it shows up.
A Okay.
Q So, Dr. Etminan, you rely on this

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study with respect to your opinion -- your opinions with respect to colorectal cancer?
A Right.
Q But you criticize the study with respect to your opinion for gastric cancer. Do you recall that?
MR. NIGH: Object to form.
BY MR. GALLAGHER:
Q And feel free to refer to Pages 17 and 19 of -- of your report, which is Exhibit 5.
A Yes, just give me a second.
So my criticism was, again, for, I believe, competing events -- lack of control for competing events. Patients end up dying before getting stomach cancer. You could argue it's -- you know, it could be --
THE COURT REPORTER: I'm sorry. I'm sorry. Can you speak up and repeat that, please?
THE WITNESS: So my criticism was a lack of controlling for competing events for -- for death due to other causes. If patients died earlier, they -- you know, some patients could have died early and not get stomach cancer. One could argue it's the same -- it

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could be the same for colorectal cancer patients. But it's also possible that those patients were followed up over longer periods. We don't know.
But my other criticism is the smaller number of cases in the -- for stomach cancer is 68 in the -- for the stomach cancer cases, and for colorectal cancer, it's 73. 68 versus -- I'm reading that off of Table 1 -- 73. So those -- those five extra cases could -- you know, could change the results. So that's what I based my opinion on.
Because -- I'm sorry. If I could just add because the -- the upper bound --
THE COURT REPORTER: I'm sorry. Doctor, I'm sorry. You're speaking with your hand over your mouth, and I'm not understanding you.
THE WITNESS: Okay. The upper bound confidence interval for stomach cancer is 1.51, so it's very wide, suggestive of a small number of cases. Whereas for colorectal cancer, it's higher. And it's significant, so the difference of these five cases could potentially -- I mean, it is possible that

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these extra five cases made a difference, but we don't know.
BY MR. GALLAGHER:
Q Well, for gastric cancer, the lower bound is 0.37, right?
A Yes, it's .037. I'm not arguing about the magnitude. It's -- it goes from very low to relatively high. I'm just saying that this very wide bound is suggestive of a small number of events. And so this study may not have had enough events to show a more precise estimate for stomach cancer.
Q Well, the lower bounds -- let's talk for a minute about what it would mean for the hazard ratio to be 0.37. What would that mean to you?
A The 3.7 hazard ratio is -- it means that it's -- it's a protective event.
Q So if the -- okay. It would be protective.
In your report -- Dr. Etminan, do you have a phone with you or anything else?
A Yes.
Q I guess I would ask that you -- okay. You're not receiving communications from anybody --
A No. No. No.

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Q -- on the phone are you?
A No. My phone was right behind my laptop.
Q Okay. Yes, please keep that set to the side.
So in your report on page Exhibit 17, you criticize the Knekt study possibly having imprecision of dietary questionnaires for quantifying NDMA from different food groups, right?
A Right.
Q And then carrying over onto Page 18, "This imprecision might have led to misclassification of the true NDMA effects with respect to cancer and might have led to null results."
Do you see that?
A Yes.
Q When you're saying that, that imprecision of the dietary questionnaires, would apply equally to the data with respect to colorectal cancer, right?
MR. NIGH: Object to form.
THE WITNESS: Not if they're not the same people answering the question. I mean, if -- if they -- if the stomach cancer cases,

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let's say -- and we don't know this, but I'm just answering your question. If the stomach cancer cases give more imprecise answering than the colorectal cancer cases, then they would have more imprecise estimate in the results because they're not the same patients.
BY MR. GALLAGHER:
Q Okay. Would you expect there to be a difference in the imprecision of -- well, I guess a couple of questions.
One, when you're talking about that, you're talking about imprecision of the actual answers to the dietary questionnaire, what foods --
A Right. So you have imprecision on what's a measurement error from the -- the study population, and then you -- I mean, you may have -- in all studies of this nature, you could have an imprecision in recording the data.
I'm just saying because they're -- they're not the same patients. You can't assume that the same thing would happen to cancer -- happen to colorectal cancer than happen to stomach cancer cases or vice versa.
Q Okay. Would you expect there to be a difference in the manner in which the foods -- the

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dietary questionnaires answered by individuals who end up with stomach cancer versus individuals who end up with colorectal cancer?
A Generally speaking, no. But again -- let me just check one thing.
Q Dr. Etminan --
A Generally speaking, no.
Q Okay. And then there's an additional possibility for error -- additional possibility for imprecision in quantifying the NDMA. And that's if the estimate that the authors used for the amount of NDMA in any specific food group, if that's incorrect, then that's going to lead to imprecision -- imprecision also. And that imprecision would apply equally with respect to stomach cancer and colorectal cancer, right?
A Yes.
Q Okay. When you make the statement here that the imprecision might have led to misclassification of the true NDMA effect with respect to cancer, you're assuming that there's an effect of NDMA on the cancer, right?
MR. NIGH: Object to form.
THE WITNESS: I'm assuming -- again, because of the smaller number of cases and the

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upper bound confidence interval, the number in the results we see is -- basically, we don't know. And so it is possible.
BY MR. GALLAGHER:
Q But what the data is -- okay.
THE VIDEOGRAPHER: Counsel, there's about 10 minutes left on this video unit.
MR. GALLAGHER: Okay. I will finish this up, and then we can take a break for lunch.
Can we mark the -- we already marked the Loh study.
THE WITNESS: What's the exhibit number on Loh?
MR. GALLAGHER: Exhibit 15.
THE WITNESS: Okay.
BY MR. GALLAGHER:
Q And I think this is similar to the Knekt paper that we were just talking about, you -- you criticize the Loh study with respect to gastric cancer. But then you rely on it for your opinions with respect to colorectal cancer. Do you recall that?
MR. NIGH: Object to form, mischaracterizes evidence.

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THE WITNESS: I don't recall. I don't recall.
BY MR. GALLAGHER:
Q Okay. If you want to look at your report on Page 17 and on Page 19?
A Okay.
Q So -- and maybe if we pull up Page 17, the second paragraph.
A Yes.
Q Okay. So you refer to imprecise estimates of the risk. Why do you consider them to be imprecise?
A Of the 1.13? Because -- because your upper bound when the -- when the upper bound is clinically can -- shows a clinically significant risk and you have an end point interval which goes from .81 and the relative risk is 1.13. So it's, you know, it's not large, but it's a 13 percent increase. That means, it's -- it's an imprecise estimate. And then if you look at Loh's number of gastric cancers, that also kind of brings the message home, because they only had, I believe, 55 -- I'm just trying to look at it -- what was Loh number again, sorry, the exhibit number?
Q 15, Exhibit 15.

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A They only had 64 cases where, you know, in other cancers -- like others in the "other cancer" category, you have 1,462 cases. For stomach, you only have 64. So that's why I said it's imprecise.
Q So would you -- you're referring to the upper bound and the lower bound?
A Yeah.
Q And you said where the upper bound is showing a potential association that that's what you're considering to be imprecise --
A I would say -- I wouldn't say association. It shows a risk of 1.57, which is clinically significant. If it was 1.2, then one would say well, even the upper bound of 1.2 is not that big of a deal. But 1.57 makes it significant.
Q How are you -- how are you deciding that 1.2 might not be clinically significant but 1.57 might be clinically significant?
A I mean, usually anything below 1.5, we think that -- and closer to 1 is significant of no risk. And the higher, from 1.5 to even higher, is suggestive of -- if it's the upper bound and it's imprecise, I would say, if it's above an increase in risk that's imprecise, that needs to be looked into,

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or inconclusive basically.
Q Okay. You would agree with me that if there is no association between an exposure and a risk, you would expect the observed relative risk to be close to 1, right?
MR. NIGH: Object to form.
THE WITNESS: I don't -- I don't want a say yes. That's a very, very general statement. There are large -- very large studies done with relative risks of 1.15 or 1.16 that is -- where the results have been taken seriously. So I don't want to say yes as a general statement.
THE VIDEOGRAPHER: Counsel, there's about 3 minutes remaining.
MR. GALLAGHER: Okay. Let me finish this up, and I'll take a break.
BY MR. GALLAGHER:
Q I guess my question was slightly different. If there is no association between an exposure and a risk, start from that assumption, you would expect the observed -- the observed relative risk to be close to 1, right?
MR. NIGH: Object to form.
THE WITNESS: If you knew -- if you

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knew there isn't an association?
BY MR. GALLAGHER:
Q You know there is not an association between the exposure and the risk --
A Right. Right. I want -- right. So the relative risk has to be close to 1 and the upper -- the -- the confidence intervals also have to be precise enough to exclude a risk, right?
So -- so if you tell me there is a relative risk of 1.2 with a confidence interval of 1.9 to 1.3, that -- that would tell me that, yes, there's probably no risk associated. But with an upper bound of 1.57, I would like -- you know, I'm more comfortable saying this is an inconclusive study rather than a no risk or a negative study.
Q But you agree that the data, the confidence interval is -- is going to or can include both below 1 and above 1 if there's no association? In fact, you might expect that?
MR. NIGH: Object to form.
BY MR. GALLAGHER:
Q Correct?
A Well, precision, if I wanted -- if I want to decide on risk or no risk, precision is also important because you could have -- again, as I

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think you mentioned, you could have a low relative risk that has a huge confidence interval. Actually, that -- that is more inconclusive than negative. If it's a relative risk close to 1 with a very tight confidence interval also close to 1 or below 1.5 for the upper limits, that is -- yes, that -- I'm more confident in that case that there is no risk.
BY MR. GALLAGHER:
Q Where are you coming up with this -- this limit of 1.5?
A 1.5 or higher, not just 1.5. 1.5 or higher.
Because it's -- it's technically a 15 percent increase that -- that is included in that interval. And one should, you know, do a further investigation to further look at that. I don't think it's -- it's high enough to warrant further investigation with a bigger study, you know, higher number of cases. It is not a definitive negative with those numbers.
MR. GALLAGHER: We can go off the record now.
THE VIDEOGRAPHER: The time is now 12:49. This ends Media Unit Number 3. We're going off the record.

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(Whereupon, a lunch recess was taken.)
THE VIDEOGRAPHER: The time is now 1:30. This begins Media Unit Number 4. We're back on the record.
BY MR. GALLAGHER:
Q Welcome back, Dr. Etminan.
A Thank you.
Q Did you have a good lunch?
A Not bad.
Q Excellent. In part of your report, Dr. Etminan, you go through a Bradford Hill analysis?
A Yes.
Q Is a Bradford Hill analysis something that you do in your professional capacity outside of serving as an expert for litigation?
A I mean, I use the criteria set by Bradford Hill to when I'm looking for -- or asking questions as part of my research on whether Drug A causes, you know, outcome Y, because I feel like it is relatively complete, and it has a lot of the sort of variables that one needs to consider when deciding on a cause --
THE COURT REPORTER: On a cause of what?

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THE WITNESS: Causal question.
THE COURT REPORTER: Thank you.
BY MR. GALLAGHER:
Q Have you published papers that present the Bradford Hill analysis?
A I can't remember off the top of my head, but most of my papers are original research, which means I am -- I am not really asking a causal question based on the available evidence. I'm asking a causal question, say, on the drug that's never been asked before. So, you know, the Bradford Hill doesn't necessarily apply to those types of questions. But I have used it as part of my research when I'm reviewing a topic.
Q So when you say most of your research -- I will ask you a new question. Strike that.
When you say most of your research is the type of research that Bradford Hill wouldn't apply to, why is that?
A Because Bradford Hill, again, is a method used to establish causality on questions where there is evidence already. And so one uses this criteria with that evidence to see whether there's a causal link between that drug and that

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outcome.
If I'm doing an original study where no one has looked at the question, you know, before, or there isn't a lot of evidence and I am the actual -- the only person or the very few people who are actually trying to answer the question, then the Bradford Hill doesn't really apply to these types of original research studies.
MR. GALLAGHER: I'd like to mark as the next exhibit, Exhibit 19, an article by Bradford Hill that you cited in your report. Let me know when it shows up.
(Whereupon, Exhibit 19 was marked for Identification.)
THE WITNESS: Okay. Oh, sorry. I'm still -- I'm still waiting.
BY MR. GALLAGHER:
Q Okay. Did it just pop up now?
A It did now, yeah.
Q Okay. If we can share the first page of this article. So this is an article by a professor from the University of London, Sir Austin Bradford Hill, right?
A Right.
Q And the title of the article is, "The

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Environment and Disease Association or Causation," right?
A Right.
Q And this is -- the article originally -- this is a republication of an article first published in 1965 where Sir Bradford Hill lays out the factors that he feels are appropriate to evaluate in assessing the causation question, right?
MR. NIGH: Object to form.
THE WITNESS: Yes.
BY MR. GALLAGHER:
Q You agree with me that association is different from causation, right?
A Generally speaking, all the causations are associations, but not all associations are causations.
Q All right. Can you say that again?
A All causations are associations, but the reverse is not true; so not all associations are causations.
Q Okay. I just wanted to make sure that I understood you properly.
So those are -- there can be associations that are observed where there's not a causal connection between the exposure and the

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result?
A Yes.
Q Correct?
A That's called an association, yeah.
Q And the numbers -- or the variables that we have been discussing today, like relative risk and hazard ratio, those are a measure of association, right?
A No, those are measures -- or they are measures of effect. So you could have an effect of, let's say, a hazard ratio of 10 that's -- from a study that only shows an association, or it can show a hazard ratio of 10 from a study that shows causation.
So the hazard ratio and the rate ratio is mainly the effect size, the -- the -- the magnitude of the effect. Whether it's an association or a causation comes to, you know, the variables discussed by Bradford Hill and also, you know, presence of confounding and all the other principals that we've discussed.
Q Okay. And when you say it's a measure of the magnitude of the effect, it's -- the hazard ratio, as a variable being measured, is not of itself measuring causation. You have to go through

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the...
A One of the criteria set by Bradford Hill and also --
THE COURT REPORTER: And also the what?
THE WITNESS: There has to be an effect from the exposure to classify whether it's a -- you know, if it's -- if a drug is -- has a relative risk of 1 with respect on outcome, that drug is not causing that outcome. So that -- that magnitude has to be more than 1.
But on top of that, that -- you know, that magnitude that's greater than 1 also has to have other criteria that Bradford Hill has talked about to be classified as a causal link.
BY MR. GALLAGHER:
Q Okay. Looking at the -- the first page on the right-hand column going through the nine factors that Bradford Hill lists, the first factor he lists is strength. Do you see that?
A Yes.
Q And so is this what -- what you're referring to in terms of the greater the magnitude of the association, the more evidence there is that

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the association may actually be a causal relationship?
A Right. It's one of the criteria, yes.
Q It's just one of the criteria. Okay.
And Sir Bradford Hill gives an example of an association -- occupations of patients with scrotal cancer versus occupations of patients presenting with other diseases. And the mortality of chimney sweeps --
THE COURT REPORTER: I'm sorry. The mortality of what?
BY MR. GALLAGHER:
Q Of chimney sweeps from scrotal cancer was some 200 times that of workers who were not specially exposed to tar or mineral oils. Do you see that?
A Yes.
Q And so that's an example of a strong association where the magnitude of the observed association is high enough that it's much more suggestive of a causal relationship, right?
A Right.
Q And so if we're looking at hazard ratios that are perhaps above -- the observed hazard ratio is above 1, it's like 1.5, that's less

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suggestive of a causal relationship without -- without more, right?
MR. NIGH: Object to form.
THE WITNESS: Again, I disagree. It's not a -- it's not a one-size fit all sort of assumption to make. A hazard ratio of 1.5 that meets the other criteria set by Bradford Hill and also other -- it also satisfies, you know, minimal bias in terms of a study having a minimal amount of biases. One can still infer that there is a causal link. I mean, the 200 times is a very rare example that he mentions, and I have never seen any drug or any exposure to having 200 times of the risk. That's an extreme.
It's a good teaching example, but in real life, I have never seen anything that can cause that much of a magnitude. So that's really not a -- that level should not really be set as a -- as a sort of standard of effect sizes for causality.
BY MR. GALLAGHER:
Q Sure. I mean, additional -- Sir Bradford Hill goes on to provide an additional example of the death rate from cancer of the lung in

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cigarette smokers as nine to ten times the rate of nonsmokers. And the death rate in heavy smokers is 20 to 30 times as great, right?
A Uh-huh.
Q So that's just another example.
I guess my only question is -- is to understand how this factor is evaluated. If you have a relative risk -- observed relative risk of 1.5, that is for this factor not as suggestive for a causal relationship as if the relative risk is like for cigarette smoking, 10 times or 20 to 30 times?
MR. NIGH: Object to form.
THE WITNESS: No. I wouldn't say that, you can't -- if it's 1.5 and, again, all the other criteria have been met, I don't think you can say it's -- it's not causal. We can say that a relative risk of 10, again, with everything being checked in and checked out with all the other criteria, just talking about the effect size, a relative risk of 10 is -- is suggestive of a stronger causal link than the 1.5. But you can disregard the 1.5 risk, especially if you're making a population, because the 1.5 risk of a disease in the large population can lead to -- even though it's a

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small number, but it can -- because the population is large, it can lead to a significant number of cases. So I think, again, you can't generalize it in that fashion.
BY MR. GALLAGHER:
Q So is what you're saying is you essentially don't -- from your perspective, you don't apply this factor of evaluating the strength of the association because there -- you know, there can be an association no matter what the relative -- observed relative risk is?
MR. NIGH: Object to the form, mischaracterizes testimony.
THE WITNESS: No. I definitely look at it -- I definitely look at event sizes, but I don't have a threshold to say, you know, if it's not close to 200, then I'm not going to consider it as a causal link. I would say again, and this is -- a lot of scientists, epidemiologists, use a relative risk of 2. Some use 1.5. I would say anything greater than 1.5 that satisfies the other criteria would be -- or higher, would be -- would satisfy this effect size criteria of Bradford Hill.

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BY MR. GALLAGHER:
Q Okay. But you would agree with me that if the observed relative risk is 1.5, that you would want more additional information from the other factors to infer causal relationship than perhaps you would insist on if the observed relative risk was 20 or 200?
A Again, the other -- the other factors are independent of the effect size. I mean, you can have an effect size of 100, but if the other factors do not satisfy -- are not satisfied, just because you have an effect size of 200, you cannot say there's a causal link because the temporality may not be there. The analogy may not be there. The biases could be there.
So again, the magnitude of effect size has to be there, but there is no set standard. And it doesn't -- it's not the only variable that we look at.
Q Okay. Moving on to on Page 33, the right-hand column, the second Bradford Hill factor is consistency?
A Yes.
Q And under "Consistency" for Bradford Hill --beneath that in the paragraph, if we

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can include the -- and the paragraph right below that as well.
So Sir Bradford Hill says that, "This requirement may be of special importance for those rare hazards singled out in the section's terms of reference," right?
Do you see that?
A Uh-huh.
Q What is your understanding of how the -- this factor of consistency is applied?
A Again, I think Bradford Hill, as you have it on -- on the screen, he mentions is -- he means by consistency, has it been repeated in different persons, in different places, circumstances. So is it perhaps consistent with being observed or seen?
And so that's -- that's what I also take -- take it to mean, that is this -- is this effect that I'm seeing, has it been seen in other settings or in other studies. It doesn't mean that it has to be observed in every single study, but is it -- is it just a one-time event, or is it being observed in other settings as well.
Q Okay. And so that would be like, for example, there's -- where there's multiple studies

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designed in different ways that are showing -- that are showing the same relationship, right?
A Yes. And I also would include even animal studies as well, because they also -- I mean, I know that's far more biologic plausibility. But if there is studies repeating -- like, repeatedly showing that there is cancer within carcinogenic animal studies, I think that should also be part of consistency as well.
Q Okay. And if you see over on Page 34, the next page, the top -- the left-hand column at the top, again discussing consistency, Sir Bradford Hill says, "I would, myself, put a good deal of weight upon similar results reached in quite different ways, e.g., prospectively and retrospectively."
Do you see that?
A Yeah.
Q And so from -- from his perspective, looking at studies, both studies that may be looking retrospectively but also studies that are being done prospectively, is significant to him in terms of determining whether an association -- whether this factor of consistency is met, right?
MR. NIGH: Object to form.

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THE WITNESS: Yeah.
BY MR. GALLAGHER:
Q The third factor over on the right-hand column of -- of this Page 34, specificity?
A Yes.
Q And this factor -- and this factor is looking at whether there's a specific association between the -- disease and an exposure; is that right?
A Yes.
Q And then at the bottom of Page 34, the fourth factor is temporality. So this is a question of -- of timing, right?
A Yes.
Q Does the -- does the exposure come before the outcome, right?
A Yes.
Q And with respect -- when -- when the outcome that you're looking at is cancer, for -- for temporality a part of the question would be does the exposure come before the subject gets -- gets cancer, right?
A Yes.
Q And there's also, specifically with

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respect to cancer, because it can be slower to develop, typically subjects are exposed to many factors, including environmental factors, that come before they develop cancer?

MR. NIGH: Object to form.

THE WITNESS: Well, I mean, temporality is just focusing on does the exposure come before the outcome, really. It's not talking about one exposure, different exposure. It's -- I mean, obviously, if -- if the exposure came after the outcome, then that's -- there's no causal link. So there has to be -- the exposure has to come before the outcome to -- to show a cause and effect relationship.

BY MR. GALLAGHER:

Q Okay. Going on to Page 35, the fifth factor is called biological gradient.

A Yes.

Q This is referring to essentially a dose response relationship; is that right?

A Yes.

Q That the greater the level of exposure -- if the -- if the risk of the outcome increases with increase in the level of exposure,

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that can be one -- one factor that is indicative of a causal relationship, right?

A Yes.

Q Moving on to the bottom of that column, the sixth factor is plausibility.

A Yes.

Q For this factor, it's just a question of is the -- is there a suggestion that it's biologically plausible that the exposure is associated with the outcome -- or that the exposure is a causation of the outcome, right?

A Yes.

MR. NIGH: Form objection.

THE WITNESS: It asks -- it basically asks is there a plausible mechanism for this cause to -- for this exposure to cause the outcome.

BY MR. GALLAGHER:

Q Okay. And then the -- the -- moving on to the right-hand column of Page 35 the seventh factor is coherence. In your mind, how is coherence different from plausibility?

A So coherence to me is whether -- whether there is a length between the plausibility, the basic science studies, and the --

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THE COURT REPORTER: I'm sorry. The what and the clinical studies?

THE WITNESS: If -- if there is a -- if there is a link or there is a nice flow, if you will, from the basic science animal studies and the clinical/epidemiological studies.

BY MR. GALLAGHER:

Q Okay. Moving on to the bottom of this, Page 35, in the right-hand column, the eighth factor is experiment. And essentially this is looking for experimental evidence, right?

A Yeah.

Q And that's experimental evidence that's different from -- it's not looking at an observational study but a true experiment or randomized control trial, right?

MR. NIGH: Form objection.

THE WITNESS: Yeah. I mean, again, I don't think it's clear enough on that, but most people take it to mean that it means a true experiment and, you know, in a randomized trial or an RCT.

Q And then on -- going on to Page 36, the ninth -- the ninth factor is analogy, right?

A Yes.

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Q And this is just a question of are there -- I guess, what's your understanding of how this factor of analogy is applied?

A I'm just going to refer to my report just to refresh my memory.

Q Sure. It's on Page 27.

A Right. So analogy means that is there any evidence that carcinogens that are similar chemically, you know, similar in the chemical structure of the carcinogen in question also cause cancer. So sometimes people refer to it as a class effect, for example. So if one drug can cause an adverse event, then that -- sometimes, it's a class effect so that the group of drugs in that class of drugs can also cause that adverse event, which strengthens the analogy -- analogy argument.

But it generally means whether -- if we talk about the carcinogen, whether other carcinogens that are similar in structure also -- have also shown to cause cancer.

Q Okay. Let's go up ahead and pull up your report, section -- report Page 29, and we can look at the table. And if you want to refer back to Pages 27 or 28, please -- you know, please feel free to.

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So I guess -- Sir Bradford Hill presented these -- one question -- Sir Bradford Hill presented these factors in a -- in a particular order. The first being strength, then consistency, then specificity, then temporality, then biological gradient, then plausibility, then coherence, then experiment and then analogy, right?

A Right.

Q And you haven't followed that -- that pattern. Is there any particular why -- particular reason why?

MR. NIGH: Form objection.

THE WITNESS: No, I don't think -- I don't think the pattern is important. I think it's the presence or the status of these variables that's important, not -- not -- I mean, it's not a temporal exercise. It's whether this variable exists, whether an analogy exists, whether temporality exists.

BY MR. GALLAGHER:

Q Okay. With respect to -- with respect to the data that's in here, you've only included the Hidajat study, right?

A Yes.

Q You haven't included the studies or

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referred to the studies that suggest that there may -- that there was not a statistically significant observation of an association, right?

MR. NIGH: Form objection.

THE WITNESS: Again, we have talked about statistical significance. It's not a -- it's not a -- statistical significance has not -- has nothing to do with the Bradford Hill criteria.

I have included the Hidajat because I felt that it satisfies this criteria more than the -- in this table. But I have included the -- the data from the dietary studies in my assessment from all the variables as well.

BY MR. GALLAGHER:

Q And the data -- the data that you're showing for strength of evidence, I guess -- where are you getting that data from? That's just -- strike that.

The data that you're presenting for strength of evidence is just the odds ratios that were reported from the Hidajat study, right?

A It's the hazard ratios of the highest versus lowest NDMA categories.

Q From the Hidajat study, right?

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A Yes. Yes. It actually says in it on the -- on the bottom of the table.

Q Sure. So are you looking at the first footnote, I guess, where there's the carat?

A Yes.

Q The numbers are --

THE COURT REPORTER: I'm sorry. The numbers are what?

MR. GALLAGHER: Numbers are from the study by Hidajat only.

BY MR. GALLAGHER:

Q Is that correct?

A Yes.

Q And that carat is actually next to dose response. And dose response is presented -- these data I think as you said, is the hazard ratio of the NDEA --

A Yes. I mean, the dose response analysis is -- is the strength of the evidence, because they only, pretty much, did a dose response. So they -- they don't have a category of just other use -- you know, other risks of cancer with NDMA. They looked at a dose response, so that's -- that's why I could see the numbers duplicated because they're pretty much the same.

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Q So you essentially treated those -- you treated those factors as the same, not different?

A Right.

MR. NIGH: Form objection.

BY MR. GALLAGHER:

Q In evaluating coherence, if we blow up on Page 29, Section IX, which is just above the table.

A Yes.

Q So you explain that from your perspective, coherence examines whether there's a link or coherence between basic science and epidemiological evidence, right?

A Yes.

Q And then in your -- but then in applying that, you say, "All nine cancers have been shown to have a causal link from well-designed large epidemiologic, occupational and scientific studies."

It seems like you're assuming a causal link from the epidemiologic, occupational and scientific studies, right?

MR. NIGH: Form objection.

THE WITNESS: Well, that's -- I mean, that's -- that's where my -- I mean, I talk

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about this in my opinion. Here, I use the word "causal" because they -- you know, if you look at the strength of the -- of the evidence and ratios and also the other -- the categories of Bradford Hill, they do satisfy the -- the different categories. And that's why I -- I use the word "causal."

Because when you get to coherence, then I have also looked at biologic plausibility, and analogy and all the other -- this -- this is the last criteria. So I have already looked at all the other criterion and have, you know, determined my -- my opinion that I do believe there is causal link.

BY MR. GALLAGHER:

Q So you're not applying coherence. By the time you get here, you've decided there's a causal link, and it's based specifically on the strength of the association. That's what you said?

MR. NIGH: Form objection, mischaracterizes his testimony.

THE WITNESS: No. I disagree with that. By the time I got to coherence, I have looked at the other criteria as well.

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BY MR. GALLAGHER:

Q Right. But how -- how are you applying coherence here?

MR. NIGH: Form objection.

THE WITNESS: I am -- I am -- I'm stating that there -- because there is a link -- there is a causal link in terms of strength, temporality, biologic plausibility, that satisfies the coherence or the flow between the basic science data and the clinical data.

BY MR. GALLAGHER:

Q Okay. The data that you had looked at, though, were epidemiologic, occupational -- well, let's break those down.

Epidemiologic and occupational studies, so those are like the Hidajat study, Straif study, right, the occupational studies? Those are a couple of occupational studies that you looked at?

MR. NIGH: Form objection, incomplete question.

You can answer.

THE WITNESS: And -- and the dietary studies, yes.

BY MR. GALLAGHER:

Q Okay. So the dietary studies would be

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epidemiologic studies; is that right?

A Yes.

Q Okay. The dietary studies are not occupational studies, right?

A No.

Q What are the basic scientific studies that you're --

A Those are the animal studies that have shown NDMA can cause cancer.

Q If we go back to Page 28, looking at consistency, it's labeled VI.

A Uh-huh.

Q So, again, explain to me how you -- how you've applied consistency here?

A Consistency means that there is basic science evidence suggesting of cancer, the causing -- the cancer-causing effects of NDMA in animals, and the occupational studies, mainly Hidajat. And many of the dietary epi studies have also shown that the -- the risk of cancer is increased. So that's the consistency.

Q So you say -- you say, mainly Hidajat. And in terms of consistency from Sir Bradford Hill, it seems like he was wanting -- be wanting to look at all of the studies, including studies that were

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prospective and retrospective, right?

MR. NIGH: Form objection.

THE WITNESS: Hidajat was prospective, it was a prospective cohort where they followed men for 35 years. We have the dietary studies where they're a mixture, a mix of prospective and retrospective. And Bradford Hill does not say that -- he says there has to be evidence from, as you said, prospective and retrospective.

He doesn't say there has to be, you know, a consistent increase in risk in of all of the studies that you have. He's just suggesting that there has to be evidence from a mix of studies, which we do have here.

BY MR. GALLAGHER:

Q So wouldn't it be relevant to this factor of consistency, if there are studies that -- some studies show -- in some studies, they reach statistical significance or an association, but that there's other studies where there's no statistically significant association? Isn't that inconsistent results?

A Again, a statistical significant has nothing to do with either the Bradford Hill criteria

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or consistency. And I think I've -- I've talked about the caveats of interpreting statistical significance. So if you'd just give me a few minutes, and I'll just read consistency from his paper again.

Q Sure.

A I mean mainly what it says is, "I would myself put a good deal of weight upon similar results" from prospective and retrospective studies.

Again, it doesn't say that all of these results have to be consistently showing an increased risk with that particular exposure. So he's -- he's quite -- he's quite general in his statement, and we do have in this question a mixture of prospective and retrospective epi -- epi and occupational studies.

Q So I'm not following. I think you said he's not requiring that the results are consistently showing the same --

A He's not --

MR. NIGH: Hold on. Let him finish his question.

BY MR. GALLAGHER:

Q I'll start over.

I heard you to say that your

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interpretation of this, Doctor, is that Bradford Hill is not requiring that the studies consistently show the same observed association?

MR. NIGH: Objection, form and mischaracterizes his testimony.

THE WITNESS: Let me clarify. I'm just reading from what he's saying. "I would myself put a good deal of weight upon similar results reached in quite different ways, e.g., prospective and" -- "prospectively and retrospectively."

And so -- so this -- I mean, this report and the findings does meet this criteria. I have retrospective studies and prospective studies. And it doesn't talk about the statistical significance or anything like that at all.

BY MR. GALLAGHER:

Q Well, but wouldn't it be relevant -- wouldn't it be relevant to this, Doctor, if there are some studies that are concluding evidence of an association based on statistical significance, but there's other studies that are concluding no evidence of an association?

MR. NIGH: Form objection.

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THE WITNESS: Again -- the Bradford Hill criteria is a method of looking at the totality of the evidence. You're rarely going to have a situation where all the studies that you have are consistently showing at one direction with minimal limitations. You're gonna have a mixed bag.

And I think that's why his -- I mean, the bar is quite low from what he's saying. He says, I want to see the, you know, results from a mix of prospective and retrospective. He's not going into any detail about, you know, what if some of them are negative, some of them are positive, what's the statistical significance. That's -- that's not -- at least that's not how I read it.

BY MR. GALLAGHER:

Q So from your perspective, this factor of consistency, it's not relevant if, among the studies that are being -- that have evaluated the question, some of them are positive and some of them are negative?

MR. NIGH: Object to form, mischaracterizes testimony.

THE WITNESS: I think I -- I think the

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ones that have the highest weight and the stronger methodology, I think if those studies are showing an association -- plus there's, you know, evidence from animal studies. And as he says there's a mixed bag of prospective and retrospective. That to me, has satisfied his criteria.

Q So again, if there's -- if there's a mixed bag of some studies are positive and some studies are negative, wouldn't you consider that to be evidence of inconsistency?

MR. NIGH: Object to form.

THE WITNESS: In most situations, you're gonna have a mixed bag of studies, as I mentioned. If -- if you wanted to apply Bradford Hill to just questions that have only positive studies, you wouldn't -- you wouldn't be applying it a lot. So it all depends if the mixed bag, what -- you know, what -- what quality of evidence comes from those -- those mixed studies.

And here, I think that the study by Hidajat, has, you know, perhaps a high end rate. Plus the studies, the epi studies, and plus the data from animal studies, satisfy the

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consistency criteria.
BY MR. GALLAGHER:
Q Okay. Let's go to -- let's go to the exhibit we were looking at early this morning, the article you had written about personal use of hair dyes and risk of cancer.
A Can you please -- can you please upload that again?
Q Sure.
MR. GALLAGHER: Can you put that back in the chat?
BY MR. GALLAGHER:
Q Do you have it?
A Yes.
Q Okay. We had looked at this this morning, and in this paper, you walk through the way you structured the searches for this, right?
A Yes.
Q And then you established -- you established inclusion criteria for collecting the data, right?
A Yes.
Q And then you set forth the way in which you did a quality assessment of the studies that were inclusive, right? And this is on

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Page 2519. It's the fourth page of the article.
MR. NIGH: Form objection.
BY MR. GALLAGHER:
Q On the left-hand side.
Do you see that where you're describing the quality assessment that you had done?
A Yes.
Q And in that quality assessment, you came up with a series of criteria that were used to rank the quality of each of the studies; is that right?
A Yes.
Q And you would have come up with this quality assessment before deciding which -- which studies were of higher quality and which were of lower quality, right?
MR. NIGH: Form objection.
THE WITNESS: Usually, that's what quality assessments are done for, yes, used for.
BY MR. GALLAGHER:
Q Okay. Okay. You haven't described that type of quality assessment in your report for evaluating the -- the studies that you decided to include on which to base your opinions, have you?

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MR. NIGH: Form objection.
THE WITNESS: I did not, because first of all, as you can see here, we have a lot of studies, that needs to be sifted through with different methodologies. In this case, I was mainly faced with two types of studies. Hidajat was one, and then the rest are all dietary studies with dietary questionnaires and very similar design.
So I preferred to kind of describe the methodology, the limitations and strengths rather than, you know, come up with a quality -- quality score.
BY MR. GALLAGHER:
Q So you haven't gone through this -- sorry -- this -- of having criteria to evaluate these studies that you're relying on for quality, and then --
A No. And again -- another -- another reason is this --
MR. NIGH: Sorry. We couldn't hear the question because someone coughed. And that happens, I know. But can you please ask that question again?
MR. GALLAGHER: Sure. No worries.

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BY MR. GALLAGHER:
Q So you haven't -- you haven't gone through the process of having criteria to evaluate the quality of the studies that you're including in your report on which your opinions are based, prospectively to describe the quality of each of them, right?
A Right. And I believe I did reply as to why. And if I could also add, qualities -- although it was done here, and this was a quality score that we just came up ourselves, it's not a standardized quality score that's published. We just came up with it ourselves.
But there's really no evidence that a quality score would necessarily improve the quality of the review when -- you know, when the strengths and limitations of the studies in the review are discussed and sort of analyzed. And with the fact that, again, the studies are very similar in design, I choose not to use the quality score.
Q Okay. When you say "they are similar in design," I thought we had discussed earlier this morning, that all of the studies have different designs, right?
A Well --

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MR. NIGH: Form objection. Form objection.
Go ahead. You can answer.
THE WITNESS: So, you have -- you have pretty much one occupational study that I relied on, and that's in Hidajat. And I talked about that extensively in more than a couple of pages. And then -- so that's obviously different than the epi studies.
But then the epi studies are pretty much very similar in design. That's what I meant. So you have two types of designs, occupational and epi. And then the epi are very similar in design. They are all questionnaire-based dietary studies.
So if I had a number of randomized trials, a number of occupational studies, a number of dietary epi studies and number of studies on different designs, then that may have warranted a quality score.
But because of the small number of studies and -- and the -- and the fact that I felt I could describe them, the strengths and limitations and the fact that really, quality scores, although intuitively, they look -- they

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sound good for observational reviews, have not really shown to improve the -- you know, to change the quality of the review if that review does contain a formal discussion of the limitations and strengths of the studies included.
BY MR. GALLAGHER:
Q Okay. Can we look at the Straif paper again?
A Sorry, which paper?
Q Exhibit 7, Straif.
This was another occupational study looking at the workers in the rubber industry, right?
A Yes.
Q On Page 19 of your report, you're looking -- you're discussing your opinion with respect to pancreatic cancer?
A Yes.
Q And you -- you criticize the Straif study as being, in your opinion, underpowered to examine pancreatic cancer deaths, right?
A Yes.
Q And that's because there were only 15 pancreatic cancer deaths in the cohort for the

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Straif study, right?
MR. NIGH: Form objection.
THE WITNESS: Right.
BY MR. GALLAGHER:
Q So isn't it -- isn't it the case that at least for the cohort that Straif was looking at, there weren't very many members of that cohort that had pancreatic cancer or died from pancreatic cancer, right?
MR. NIGH: Object to form.
THE WITNESS: So 15 cases only.
BY MR. GALLAGHER:
Q Right. So the -- the powering of the study is -- is based largely off of sample size, and the expected size of a potential association, right?
MR. NIGH: Form. Form objection.
THE WITNESS: So there are about four criteria for the power. One of them is sample size or, more specifically, number of events.
BY MR. GALLAGHER:
Q Okay. If you look -- let's look at the Straif study, on Page 181, in the right-hand column just above the table.
A Okay.
Q Do you see where they're describing

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for this cohort, they "assessed exposure to total nitrosamine because animal studies indicated linear additive carcinogenicity for exposure to low concentrations of different nitrosamines and because assessment of exposure to specific nitrosamines would not have been possible." Right?
A Okay.
Q So for this -- for this study, assessment of the exposure to specific nitrosamines would not have been possible, right?
A Right.
Q If we go to Page 185 in the left-hand column, the -- the top, the first full sentence, they state, "We have discussed previously that the increased risk of stomach cancer among rubber workers was mostly found in work areas with relatively low exposure to nitrosamine."
Do you see that?
A What page is that? I'm trying to look at in my PDF. What page is that?
Q Sure. It's Page 185. 185, the top left-hand column. Do you see that sentence where they --
A Yes.
Q -- say, "We have discussed previously

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that the increased risk of stomach cancer among rubber workers was mostly found in work areas with relatively low exposure to nitrosamine"?
A Right. And they reference two studies. Okay.
Q So wouldn't that be inconsistent with a suggestion that among rubber workers, it was nitrosamine that was leading to an increased risk of stomach cancer?
MR. NIGH: Form objection.
THE WITNESS: First of all, nitrosamines are a more general, as you know, chemical name that includes NDMA.
And I mean, here, I'm just reading one sentence from the paper. I have to go and read the paper and see whether I believe those results or not. So I mean, that's what they're saying. I can't just go with what they're saying. I haven't reviewed those two articles.
BY MR. GALLAGHER:
Q Okay. But -- but at least these authors who are reporting in this study that you have chosen to include -- include in your report are describing that from their perspective, they have previously shown that any increased risk of stomach

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cancer among rubber workers was mostly found in work areas with relatively low exposure to nitrosamines, right?
MR. NIGH: Form objection.
THE WITNESS: Again, even -- even in this study, they only have 44 cases of stomach cancer deaths, which leads to -- you know, as expected, a very wide confidence interval.
So if -- if that study that they're mentioning is similar to this study, it may be because, again, it -- it was a very low -- in a small number of stomach cancer cases. And unlike Hidajat, it did not control for death by other causes.
So, yes, that's what they're saying, but I don't -- I'm not sure if I, you know, believe their -- their methodology.
BY MR. GALLAGHER:
Q Okay. Back to your report, Page 19 over to Page 20?
A I'm sorry. Can I just mention -- can we -- after you ask your question on Page 19, can we take a ten-minute break?
Q Sure. Absolutely.
Let me just ask this quick question,

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and then -- and then we'll take a break.
So you discount the Straif study and are relying on the Hidajat study with respect to your opinions for pancreatic cancer, right?
MR. NIGH: Form objection.
THE WITNESS: For pancreatic cancer, I also do mention the Zheng study and I mention the Fritz -- Fritschi study.
Q What's the -- what's the second study you just referred to, Fritschi?
A Yeah.
Q Well, the -- the Fritschi study, F-r-i-t-s-c-h-i, you'll agree with me did not find an association --
A That's correct.
Q -- between nitrosamines and pancreatic cancer, right?
A That's right.
Q And you discounted the Straif study, which also did not show an association of NDMA -- or of nitrosamines and pancreatic cancer, right?
MR. NIGH: Form objection.
BY MR. GALLAGHER:
Q And you do rely on the Hidajat study in support of your opinion regarding the association

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of NDMA and pancreatic cancer, right?
A And -- and Zheng.
Q Sure. Okay. I'll get to Zheng in a minute.
A Okay.
Q So -- but the Hidajat study as we discussed earlier today, was one of occupational exposure where the exposure is primarily inhalation or contact through skin, right?
A Yes.
Q Okay.
MR. GALLAGHER: Why don't we take a ten-minute break now, and we'll pick up with the Zheng study when we come back.
THE WITNESS: Sure.
THE VIDEOGRAPHER: The time is now 2:30. This ends Media Unit Number 4. We're going off the record.
(Whereupon, a short break was taken.)
THE VIDEOGRAPHER: The time is now 2:49. This begins Media Unit Number 5. We're back on the record.
BY MR. GALLAGHER:
Q Dr. Etminan, I'm going to mark as Exhibit 20 an article by Zheng, Z-h-e-n-g entitled

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"Dietary N-nitroso Compounds and Risk of Pancreatic Cancer: Results From a Large Case Control Study."
(Whereupon, Exhibit 20 was marked for Identification.)
THE WITNESS: Which exhibit is this? Sorry, 37?
Q Exhibit 20.
A Oh, 20. Okay.
Q It's Exhibit 20. It is -- you have cited it on Page 20 of your report, and it's Reference 37 from -- from your report.
If we go to Page 258, Table 2?
A I'm sorry. Can you just give me 30 seconds to find this in my report?
Q Sure. It's on Page 20 of your report.
A Oh, 20, okay.
Q And if you want we can -- sorry to -- we can --
A On Page 20 is -- on Page 20, I talk about Zheng and Straif, Loh. I don't see Jane.
Q Z-h-e-n-g.
A Oh, Zheng.
Q Sorry. My apologies if I'm mispronouncing it.
A That's all right.

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So it's number, which one, sorry.
Q It's Exhibit 20.
A Is it uploaded?
Q I believe it is now.
A All right.
Q Do you see it?
A Yes, I see it.
Q Okay. If we go to Page 258, Table 2.
A Yeah.
Q And Table 2 is presenting "Adjusted odds ratios and 95 percent confidence intervals for pancreatic cancer risk according to quartiles of consumption of certain N-nitroso compounds," right?
A That's right.
Q And if we -- if you look down to NDMA, the adjusted odds ratio for NDMA exposure as -- in association with pancreatic cancer is 0.13, right?
A Yes.
Q That's essentially evidence of no association between exposure to NDMA and risk of pancreatic cancer in this study, right?
A For the general NDMA, yes.
Q Okay. For the general NDMA. And then if we look at -- it also separately presents an odds ratio for NDMA from plant source, right?

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A Yes.
Q And the adjusted odds ratio for NDMA from plant sources is 1.93; is that right?
A Yeah.
Q And then separately, it breaks out NDMA from animal sources and the adjusted odds ratio for risk of pancreatic cancer and exposure to NDMA having an association of 1.7, right?
A Right.
Q So for exposure to NDMA from animal sources that's, again, evidence of no association between exposure to NDMA from animal sources and risk of pancreatic cancer, right?
A Yeah.
Q So don't you think these results are -- at a minimum, the results for plant NDMA from plant sources are inconsistent with the results for NDMA and results for NDMA from animal sources, right?
MR. NIGH: Form objection.
THE WITNESS: It is inconsistent, but I think that's something that should be -- I mean, you can't disregard it. I mean, they are -- they are not consistent. But if you can't -- you can't disregard the fact that

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there is a signal with plant sources, but of course, not with NDMA from animal sources.
BY MR. GALLAGHER:
Q Okay. And -- and we also can't disregard that the data for NDMA is showing no association of exposure to NDMA and risk of pancreatic cancer, right?
MR. NIGH: Form objection.
THE WITNESS: Well, it -- it -- it shows -- it doesn't show a risk for general NDMA, right.
BY MR. GALLAGHER:
Q Okay. You'd agree with me that the exposure to NDMA from valsartan is not exposure to NDMA from plant sources, right?
MR. NIGH: Object to form.
THE WITNESS: And it's not from animals either. But I mean, the molecule -- the molecule is the molecule. So I don't know if -- whether it comes from the plant -- I mean, it comes from the plant. But in the body, it gets broken down to the chemical NDMA. So whether it comes from a plant or any other source, I don't think that really matters that much.

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It's just like, you know, getting protein from dairy or from meat. Once it's broken down to its amino acids, it's -- it's protein in the body. It does what it's supposed to do.
BY MR. GALLAGHER:
Q Okay. Do you have any explanation for why they might observe from plant sources NDMA, a hazard ratio of 1.93, but for NDMA generally and NDMA from animal sources, there's no evidence of association?
A I -- I don't. But again, I think that it -- I mean, it is a piece of evidence that should be looked at in -- in -- in the grand scheme of all the evidence. And that's why I did talk about it in my report. I mentioned that no association with animal studies -- with the animal sources, but also did mention with the plant sources.
So I think it's one piece of the puzzle that should be -- should be looked at. If -- if the plant source was also a negative, then I would say we can disregard it. But since the plant source does show a signal and maybe we can't really explain why. But we can't really disregard the signal.

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Q So you said if the plant sources were negative, then we could disregard it. Are you disregarding studies that show no association?
MR. NIGH: Object to form, mischaracterizes testimony.
THE WITNESS: No, but what I meant to say is that if the plant source was also -- was showing a negative association, we could say that NDMA in the study does not show a link. But -- but it -- but it does show a link from plants and not animals. So we can't totally disregard it because of that reason.
BY MR. GALLAGHER:
Q Okay. Is it possible that there's some unmeasured confounding factor for those who are getting NDMA from plant sources that explains the inconsistency in this data?
A I mean, I can't think of a measured confounder that only affects plant users, but I mean, I don't know. I -- I wouldn't speculate.
Q Is it possible that there's some factor for which there's an interaction with NDMA that those who are -- have a diet higher in plant sources than NDMA have -- that hasn't been measured here, and that's creating the inconsistency in the

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results?
A I mean, I -- that's the next -- I don't -- again, I don't want to speculate. It's not really within my expertise to -- to opine on.
Q Okay. So getting back to your report with respect to pancreatic cancer, as we talked about on Pages 19 and 20, you cite to the Fritschi article?
A Yes.
Q Which reported no association of nitrosamines and pancreatic cancer.
You cite to the Straif article, which again found no evidence of an association between nitrosamines --
A Again, just to clarify, Straif was inconclusive because of a very small number of cases. And Fritschi, I do explain the limitations in my report.
Q Right. Okay. But neither of those -- neither of those are supportive -- are evidence for an association of NDMA with pancreatic cancer, right?
A Correct.
Q And then you cite the Hidajat study, which we have discussed previously, right?

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A Yes.
Q And then the Zheng study, which we've just looked at, for NDMA generally, is showing no evidence of an association of NDMA and pancreatic cancer, right?
A For general NDMA, yes.
Q Okay. So you've cited four articles. Three of them have no evidence for an association. One of them where the mechanism -- method of exposure was through inhalation or skin contact more than oral.
And it's essentially on the basis of that -- that one study that you're concluding the dietary and occupational evidence demonstrates an increase in the risk of NDMA and NDEA with pancreatic cancer, right?
A Yes. So I say the -- so I say the constellation of animal studies, the -- the large occupational studies that probably has a higher rate in terms of methodology and one increased risk of NDMA plant-based on one study. I'm kind of looking at the totality of the evidence for that.
THE COURT REPORTER: Counsel, I'm sorry. I need to just -- I need to take one minute.

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MR. GALLAGHER: Okay. Can we go off the record?
THE VIDEOGRAPHER: The time is now 3:02. We're going off the record.
(Whereupon, a short break was taken.)
THE VIDEOGRAPHER: The time is now 3:03. We're back on the record.
Mr. Gallagher, I think you're on mute.
MR. GALLAGHER: Sorry. Thank you.
BY MR. GALLAGHER:
Q Dr. Etminan, I want to explore this concept of totality of evidence with you.
A Okay.
Q So with -- with respect to pancreatic cancer, you have cited to three studies that show no evidence of an association of NDMA with pancreatic cancer. And you cite to one article again where the method of exposure was primarily inhalation or skin contact, not oral.
And based on that one study, you're telling us that the totality of evidence is supportive of an association of exposure to NDMA and the risk for pancreatic cancer; is that right?
A So --
MR. NIGH: Object to form.

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Hold on. Let me make my objection, please.
Object to form, and mischaracterizes testimony.
THE WITNESS: So totality doesn't mean just looking at what -- how many positive studies you have and how many negative studies you have. First of all, I -- I included three negative studies because they included my -- they met my search criteria in my report. And so I had to talk about them, and I -- they were negative, and I had to talk about the limitations.
And one of those three studies is Straif that -- that you mentioned, could not -- with 15 cases, could not really study the question. So it wasn't really a negative study. It wasn't a well-designed study that led to a negative results. It was a very small study that could not answer the question.
Fritschi also combined different exposures. I talked about the limitations of that study. And the -- when I say totality, yes, I believe that the study by Hidajat carries more of the weight because it was very

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long follow-up, good sample size. Yes, it wasn't oral NDMA. I don't think we could ever have an oral -- orally-based NDMA exposure study that's well designed and can follow patients for a long time. I think logistically and ethically, that's impossible.
But the -- over time, the data that we have from animal studies and other data over time, exposure to skin and lungs can lead to systemic absorption of NDMA.
So to answer your question, it is not just three negative, one positive, I decided on the positive. It's -- it's the quality of the event. It's the weight of the evidence that goes into that decision.
BY MR. GALLAGHER:
Q Well, wouldn't the dietary studies be looking at oral -- oral exposure to NDMA to the extent they're being based on assumptions of the estimates for the amount of NDMA in particular foods?
A Yes, they do. But, again, they also have limitations that, for example, Hidajat did not. And then most of their limitation would be -- that's why potentially it's that some of them are negative

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is the -- the follow-up was not as long as Hidajat to -- for -- to allow cancers to form.
And they did not control for competing deaths or deaths of other causes. So if somebody died of a heart attack, they were out of the study. They could not get cancer. That would lead to a smaller number of cancer cases.
So, yes, the dietary studies may -- may mimic -- may better mimic the valsartan scenario, but they -- they have other limitations that -- that may prevent them from showing a -- you know, an effect -- an increase in risk with NDMA and cancer.
Q Okay. Understanding that the dietary studies do have limitations, and I think we had discussed some of those earlier today, one of the -- one of the limitations of Hidajat study is that the method of exposure -- strike that.
With respect to assessing exposure to NDMA from valsartan, which would be oral, one of the limitations of the Hidajat studies as a -- as a basis for evaluating that question, is that the method of exposure is primarily inhalation or direct contact with skin, not oral exposure, right?
A Yes, I think we talked about it.

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Q Okay. Moving on in your report to head and neck cancers?
A Okay.
Q So the first -- the first study cited here is Loh, L-o-h.
A All right.
Q And for this, the observed relative risk is 1.13; is that correct?
A Yes.
Q And this is exhibit -- the article is Exhibit 15, if you want to look at it. But at the moment, we can just look at Page 20 of your report.
A Okay.
Q So you agree that that was not statistically significant evidence for an association of NDMA and esophageal cancer, right?
A Yes.
Q Okay. And the confidence interval is from 0.77 to 1.68, right?
A Yes. And, again, we have talked about imprecision and the very low and very high limits and what that means. But, yes --
THE COURT REPORTER: But, yes, what?
THE WITNESS: It wasn't statistically significant.

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BY MR. GALLAGHER:
Q In your report, you focus on the upper bound of that confidence interval. I want to talk for a minute about the lower bound of the confidence interval, 0.77.
So the -- according to this data, it would be the -- the likelihood of the actual relative risk being 0.77 is as good as the possibility that the actual relative risk is 1.68. Do I understand that right?
A I -- I don't -- I don't think I agree with that. But I do agree that it's -- and you can say it's an inconclusive result. I don't know if the probability of getting .77 is the same. I mean, it could be similar. It could be a bit -- I can't -- that's a technical statistical question. I can't -- I have to, kind of, maybe, go back and look at it.
But for the purposes of our discussion, I'm comfortable in saying that it's -- because it goes from very low to very high, that it's inconclusive. But, again, if it went from very low to, let's say, 1.2, 1.3, I would be more comfortable saying it's negative. But because it's going all the way up to 1.68, I'm more comfortable

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in saying it's inconclusive.
MR. NIGH: And I would object to the form of that last question.
BY MR. GALLAGHER:
Q If we look at Exhibit 15, the Loh study, turning to Page 1057, I believe, just below Table 2 --
A Yes.
Q -- on the left-hand side?
A Table 2, okay.
Q Yeah. Sorry, just below -- just below Table 2.
A Okay.
Q And this is -- these studies are evaluating multiple cancers. So this is carrying over from the prior page where they say, "There was no significant association with esophageal and stomach cancers for all three exposures."
Do you see that?
A Which -- which -- are you looking at a table or --
Q No. I'm sorry. I'm looking just below the table.
A Below Table 2?
Q Yes. And it's -- it's going from

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the -- the sentence starts at the end of Page 1056, the prior page and carries over to Page 1057.
A Yeah. I mean, I -- I think that's also reflected in Table 5. But in Table 5, they also -- they also show the number of cases, and as I mentioned before, with 55 cases of esophageal cancer, that does not give you a very precise estimate. So, yeah, it's not statistically significant because it's probably not supposed to be this small number of cases.
Q And the small number of cases is due in part because relatively few people in this cohort actually got -- actually had esophageal cancer, right?
A Well, again, from the table, it seems, like, compared to the other types of cancer, they -- this group had a smaller -- you know, had a smaller number of cases. I'm not sure what the percentage would be. I don't think they -- they have that as to the percentage of patients in this study who had esophageal cancer. But we just have the number of esophageal cancers from the total number of cancers, and it seems to be low.
Q Let's look at -- have we already marked the Kefzei article? Exhibit 16, the Kefzei,

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article. And you're citing to this on Page 21 of your report, with respect to --
A Please hold on.
Q Okay.
A Okay.
Q Again, now the -- the observed hazard ratio is 1.15, right?
A For which cancer? Are you looking at a specific table?
Q Oh, I'm sorry. The -- I'm looking at your report. And you're more than welcome to look at it.
A 1.15, yes.
Q For esophageal cancer?
A Uh-huh.
Q You had earlier -- when you were discussing Keszei with respect to gastric cancer?
A Yes.
Q You had criticized this article because of potential misclassification and inaccurate reporting the different food intake by the subjects. Do you remember that?
MR. NIGH: Form objection.
THE WITNESS: Yes.

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BY MR. GALLAGHER:
Q Okay. That potential for misclassification applies as equally for esophageal cancer as it does for gastric cancer, right?
MR. NIGH: Form objection.
THE WITNESS: It does, but, usually misclassification that affects both groups, usually, gives no results, which we got for stomach cancer. Here, we have, you know, a statistically significant increase in risk.
So, again, there has to be a very clear mechanism as to how misclassification is causing this increase in risk where -- esophageal because usually misclassification that's non-differential just dilutes the effect, which we --
THE COURT REPORTER: Between what?
THE WITNESS: Dilutes the effect. But here, we do see a slight increase in risk with -- in Kefzei with esophageal cancer.
BY MR. GALLAGHER:
Q Well, but you don't know if -- if there's inaccurate reporting, either inaccurate recording by the study subjects of what their actual dietary intake is, or inaccurate assumptions about

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the estimates of what the actual content of NDMA is in each of the specific foods?
MR. NIGH: Form objection.
BY MR. GALLAGHER:
Q The data is going to be inaccurate. You don't know what -- what the effect is going to be.
MR. NIGH: Is that the end of the question?
MR. GALLAGHER: Yes.
MR. NIGH: Form objection.
THE WITNESS: Yeah. We -- we don't know. And, again, I'm just saying, misclassification of a questionnaire would usually lead to null -- or null results. And we don't know what could have happened here. They're different subjects.
The other -- the other potential possibility is that, again, more of the -- I'm just making this -- I'm making this inference based on epi study design and the data. It's possible that more of the cancer patients with -- stomach cancer patients -- I'm sorry. More of the patients who were followed died before they got stomach cancer versus the --

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those who got esophageal cancer probably could have survived longer to get esophageal cancer. So these are just sort of inferential possibilities based on the data and their study design that they present.
BY MR. GALLAGHER:
Q You have no basis, though, for suggesting -- for saying that the -- the people who ultimately got esophageal cancer just survived longer than the people who got gastric cancer?
MR. NIGH: Form objection.
THE WITNESS: Again, we don't have -- we are not privy to any of this data. But from the -- from the fact that they followed these patients and looked at three related cancers, they don't talk about how many died and dropped out and any control for competing, you know, events, such as death, and making an inferential sort of suggestion that these could be possibilities. Yes, of course, I don't know. I don't think anybody would know unless you actually had access to the data and could -- you know, could analyze the data and ask more questions.

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BY MR. GALLAGHER:
Q Okay. And then in your -- in your report, again on Page 21, you go on and discuss the Straif study and the Hidajat study, right?
A Yes.
Q Neither of those studies controlled for alcohol use, correct?
A No. But, again, my analysis for one unmeasured confounder, which could be alcohol, showed -- with using the E-value that we talked about earlier, showed that the effect of that one unmeasured confounder, that could be alcohol, has to be very large to make the results, you know, not -- you know, take the results to 1, basically.
So they did not -- they did not control for alcohol in their study. But, again, I'm using a simulation. I have shown that one unmeasured confounder would not have changed the results.
Q Okay. Well, alcohol is a strong risk factor for cancer of the pharynx, larynx and esophagus, right?
A Right. And, again, remember, based on our discussion, the risk factor is not as detrimental as a confounder. In this case, it

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actually is a confounder for -- for esophageal and stomach cancers. And that's why it could fit that unmeasured confounder scenario that I show, you know, what happens if you have that unmeasured confounder and how much -- how strong that confounder has to be to make the results known.
So in a way, I did simulate for it -- but it was -- it was not controlled for in the study.
Q Okay. And the same for -- for smoking. The Straif study didn't control for smoking, right?
A The -- the Hidajat study simulated --
Q That wasn't my question.
My question was the Straif study didn't control for smoking, right?
A The Straif study --
MR. NIGH: Hold on. If you can please not interrupt the witness. I don't know if he finished that last question -- answer, but please don't interrupt him going forward.
You can answer, Doctor.
THE WITNESS: No. I think I have finished my question. Let me just pull Straif again because you --

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BY MR. GALLAGHER:
Q Sure. Yup.
A So the Straif did not adjust for smoking. But again, the main problem with Straif was with 15 cases, even if they had smoking, it wouldn't have done anything because you have so -- small number of cases that, I mean, controlling for smoking would be a moot point within the data, to move the needle, if you will.
Q Okay. And the Hidajat study, as we discussed, did not directly control for smoking, correct?
A They did not directly control, but they simulated smoking data in their study.
Q Okay. So now we have just talked about two factors that haven't been accounted for in these studies. In your --
A I -- I -- I sort of disagree with that.
I -- when you simulate smoking data and see if that changes the results or not, that is -- I mean, that is not -- it may not be the same as having the variable, but it -- it does -- I mean, you have to give it some weight. If it doesn't change your results, you can't just say, you know,

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they didn't control for it.
Q Okay. Well, they haven't adjusted for --
A They didn't have the --
Q None of these studies adjusted for --
A Right.
THE COURT REPORTER: I'm sorry. Adjusted for what?
MR. GALLAGHER: Alcohol use or tobacco use.
BY MR. GALLAGHER:
Q And just a minute ago, you were referring to this E-value methodology?
A Yes.
Q Magnitude of an unmeasured variable to reverse the risk, right?
A Yes.
Q What if there's two unmeasured variables?
A This methodology only works with one. It only works for one unmeasured confounder.
Q Okay. So it does -- it doesn't work if there's multiple unmeasured confounders?
A It does not, but, again, when you talk about confounders, as I talked about earlier -- I

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mean, alcohol use in gastric cancer and -- and in this question is a true confounder.

But there may be other variables that may look like a confounder. They may not be actual confounders. And the fact that they're not controlled for does not necessarily mean that had they been present, they would have changed the results, again, because you could have a classic confounder. But if the prevalence of that confounder is very low or its association with the outcome and the exposure is very low, it may not affect the results at all.

So I think it's a bit premature to say I don't want to believe these results because they didn't control for these unmeasured confounders. It's something to think about and sort of factor in, but I think there are caveats to it.

Q Okay. And then moving on in your report, you also address the Knekt study?

A Yes.

Q Do you see that towards the bottom on Page 21?

And you would agree with me that Knekt did -- did not find statistically significant evidence of an association between exposure to NDMA

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and risk of head and neck cancers, right?

A It found an increased risk, a 1.37 relative risk that was not statistically significant.

Q Okay. Okay. Talking for a minute about when you're doing -- looking at data from an observational study, in theory, if there's no association between the exposure and the outcome, the relative risk is 1.0, right?

MR. NIGH: Form objection.

THE WITNESS: Yes, that's possible.

BY MR. GALLAGHER:

Q Well, is it possible, or is that --

A I mean, no. That -- that scenario -- that scenario is possible that you could have -- you could have no association in a study with a relative risk of 1.0.

Q Okay. I'm -- if -- if -- by definition, if there's no association between an exposure and an outcome, the relative risk is 1.0?

MR. NIGH: Object to form.

THE WITNESS: Yes.

BY MR. GALLAGHER:

Q Okay. And if the relative -- if, in fact, the exposure is protective against having the

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outcome, the relative -- the actual relative risk is below 1, correct?

A Yeah, yes.

MR. NIGH: Form objection.

BY MR. GALLAGHER:

Q And if the -- if there's a positive association between the exposure and the outcome, the relative risk, the actual relative risk, is above 1, right?

MR. NIGH: Form objection.

THE WITNESS: Yes.

BY MR. GALLAGHER:

Q In practice, when you're looking at data from an observational study, you would rarely observe data where the observed relative risk is exactly 1.0, correct?

MR. NIGH: Object to form.

THE WITNESS: I mean, because I read a lot of papers, I have -- I wouldn't say it's that rare. I mean, it happens.

BY MR. GALLAGHER:

Q Sure. It can happen, but observation of a relative risk of data where the measured relative risk is above 1 does not mean there is an association, right?

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MR. NIGH: Object to form.

THE WITNESS: Again, you are -- you're only looking at a very small piece of the very large puzzle. I mean, one has to look at the methodology, the question, the study design, all the variables we've talked about today to be able to come up to that conclusion rather than just looking at the relative risk.

BY MR. GALLAGHER:

Q Okay. Moving on in your report on Page 22, Section 10.5 "Liver Cancer"?

A Yeah.

Q So, again, you criticize the Straif study as lacking the power to -- to examine the question, right?

MR. NIGH: Form objection.

THE WITNESS: Right.

BY MR. GALLAGHER:

Q And then you cite to the Hidajat study. That's the only other study that you cite to, right?

A That's the only other study that has looked at liver cancer, you know, in a -- as a follow-up epidemiological study that my search -- that I could find.

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Q All right. In your report on Page 22, in the Section 10.5, you don't reach any conclusions about the risk of liver cancer through NDMA exposure, right?
MR. NIGH: Form objection.
THE WITNESS: Can you repeat the question?
BY MR. GALLAGHER:
Q In your report, in Section 10.5 on Page 22 of your report --
A Right.
Q You don't reach any conclusions about the risk of liver cancer through NDMA exposure at the end of your discussion like you do for the --
A If you mean -- if you mean -- if you mean I don't have, like, a bolded summary, I -- I think it was just missed because I do have it for all the other sections. But, I mean, I do say at the very last sentence that, "To date, the study by Hidajat provides the strongest evidence on the risk of liver cancer."
Q Okay. And you -- you don't have any other studies that -- you don't -- there are -- as far as you're aware, there aren't other studies evaluating the risk of liver cancer from NDMA

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exposure; is that right?
MR. NIGH: Form objection. Do you mean epi studies or animal studies or all studies?
BY MR. GALLAGHER:
Q You're not aware of any other studies in humans with respect to evaluating risk of exposure to NDMA and occurrence of liver cancer, right?
MR. NIGH: Form objection.
THE WITNESS: I'm not aware of any human studies that met my inclusion criteria, which required, again, measurement of NDMA and demonstration of the effect size, pretty much everything I have in my inclusion criteria. I could not find a human study that would fit those criteria that I could include in my report.
BY MR. GALLAGHER:
Q Okay. And so you don't have -- you don't have any studies that you're relying on that are evaluating oral exposure to NDMA and risk of liver cancer, correct?
A No.
Q Okay. Moving on, Section 10.6 of your

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report which is looking at bladder cancer?
A That's right.
MR. GALLAGHER: Can we mark another Jakszyn article as Exhibit 21? And this is the Jakszyn article, J-a-k-s-z-y-n, Reference 48 that you're citing to on Page 22?
THE WITNESS: Right.
(Whereupon, Exhibit 21 was marked for Identification.)
MR. GALLAGHER: So let me know when that gets pulled up.
BY MR. GALLAGHER:
Q Do you see it there yet?
A I'm here, yeah.
Q Okay. So in this article -- or in this study, this study found no overall association between exogenous NDMA intake and bladder cancer, right?
A No.
Q So the observed relative risk was 1.12, right?
A That's right.
Q And the confidence interval was 0.88 to 1.4, right?
A Yes.

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Q So there's no evidence from this study of any association between NDMA exposure and bladder cancer, right?
MR. NIGH: Form objection.
THE WITNESS: I -- I do present some of the limitations of the study, but from the numbers that you cited and that I present, no.
BY MR. GALLAGHER:
Q Okay. And then back to your report, again, you look at the Straif study, right?
A Yes.
Q You cite to the Straif study, and there was no evidence or association between nitrosamines and bladder cancer, right?
A Right.
Q And then you cite to the Hidajat study in support of your opinions with respect to bladder cancer, right?
A That's right.
Q And you don't have -- those are the three studies on which your opinion with respect to bladder cancer is based, right?
A Yes.
Q And of those three studies, Hidajat was the only one where there was an observation of a

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relative risk that -- that reached statistical significance, correct?
A Correct.
Q Okay.
Moving on. On Page 23 of your report, you're looking at prostate cancer.
A Right.
Q Okay. So -- and, again, the first study you refer to is the Loh study, right?
A Right.
Q And that study, there was not a statistically significant -- not a statistically significant observation for any association of NDMA exposure with prostate cancer, right?
A That's right.
Q In fact, the relative risk was 1.01, right?
A Correct.
Q The lower bound of the 95 percent confidence interval is 0.90, and the upper bound was 1.13, right?
A Yes.
Q Would you consider that confidence interval precise?
A The confidence interval is precise,

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but that doesn't mean that the -- that the potential biases in the study that it -- that precluded the study from showing an effect. So in other words, it's not a -- it's not a very tight confidence interval coming from the very well-designed study.
So you can't just look at the precision. You have to put it into context of the -- what are the potential limitations of this study that could have led to this nonsignificant result.
Q Okay. You criticize the Loh study because it doesn't adjust for previous history of prostate cancer, right?
A Well, that's one of the criticisms. One other criticism is that they also said that overall in the population that NDMA levels is relatively low to other populations. They didn't look at high versus low NDMA, so -- so yeah, so those are the limitations.
Q Okay. The Hidajat study did not adjust for previous history of prostate cancer, right?
A It did not, but since it showed again -- because it showed a statistically -- an increase in risk, that that potential confounding

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effect of previous history of prostate cancer has to be quite prevalent in that large population, has to affect one group more than the other. So, again, just absence of or not adjusting for a non-measured confounder doesn't necessarily mean that had it been included that the results would have been different.
So here I'm just mentioning it as one limitation. But in Hidajat, because they did find the signal, I think one has to have -- has to put this into perspective, but in a different Hidajat versus Loh.
Q So you -- if it's -- if it's not adjusted for and it's an unmeasured confounder, you don't know what the effect is, right?
A We don't know what the effect is, but we know that the -- that the unmeasured confounder changes the results when -- when certain conditions are present. So if let's say, yes, they didn't adjust for Hidajat for previous history of prostate cancer, but let's say only .5 percent of the population of these men had previous history, because of that low number, adjusting or not adjusting, because of that low prevalence, would probably not have changed the results of the study.
So, again, unmeasured confounders

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changed the results of studies if -- you know, based on a number of other factors, the prevalence, their strength of association to the outcome and to the exposure.
Q Well, if -- if the -- if the prevalence of prior history of prostate cancer was that low in the population, it also wouldn't have changed the results of the Loh study, right?
MR. NIGH: Object to form.
THE WITNESS: No, it wouldn't, but again, I'm not -- I'm kind of mentioning a number of limitations and potential limitations for why Loh has that, you know, pardon the pun, low relative risk, not just unmeasured confounders.
BY MR. GALLAGHER:
Q Okay. I understand. But --
A Yeah.
Q All right. Hidajat has the same limitation.
MR. NIGH: Form objection.
BY MR. GALLAGHER:
Q Correct?
A Hidajat, yes. Hidajat does have the same limitation, but Hidajat found an increase in

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risk. And unmeasured -- and the effect of an unmeasured confounder has to be more profound to change that result.

Here, as we said, the unmeasured confounder may have been less of an issue because of the results. However, it is still a limitation that I thought I should include because, again, we don't really know, you know, have all the numbers from this study. We don't know, was it collected or not, or how it would have changed the results.

Q Sure. And you agree that we should acknowledge the limitations of studies regardless of if the result was there was an association or not an association?

MR. NIGH: Form objection.

THE WITNESS: Yes. But I mean, limitations have -- I don't -- I don't think we can paint all limitations with the same brush. There are some limitations that would not be that detrimental. There are limitations that would be.

So generally speaking, your -- I agree with your statement, but at the same time, I think there could be caveats and nuances on that statement.

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Q Okay.

THE WITNESS: Can we have a ten-minute break and come back at 4?

MR. GALLAGHER: Sure.

THE VIDEOGRAPHER: The time is now 3:50. This ends Media Unit Number 5. We're going off the record.

(Whereupon, a short break was taken.)

THE VIDEOGRAPHER: The time is now 4:01. This begins Media Unit Number 6. We're back on the record.

BY MR. GALLAGHER:

Q Welcome back, Dr. Etminan.

A Thank you.

Q Looking again at your report on Page 23.

A Okay.

Q And I'm gonna -- you'll be happy to know I'm going to move ahead to the next section, 10.8: "Blood Cancers."

A Okay.

Q So you cite a study by Richardson, right?

A Yes.

Q And Richardson is --

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MR. GALLAGHER: Well, why don't we go ahead and mark it as the next exhibit. Are we up to 23 now?

(Whereupon, Exhibit 22 was marked for Identification.)

MR. GALLAGHER: Okay. This is going to be -- the Richardson article will be Exhibit 22.

BY MR. GALLAGHER:

Q Let me know when that shows up in the chat, Dr. Etminan.

A Okay. So I have it.

Q Okay. The title of this article is "Occupational Risk Factors for Non-Hodgkin's Lymphoma: A Population Based Case Control Study in Northern Germany," right?

A That's right.

Q So this is an occupational study, right?

A Right.

Q And the -- you looked at this study and the odds ratio for exposure to nitrites, nitrates or nitrosamine, all three combined in terms of the risk factor for lymphoma, right?

A Yes.

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Q In this study, they didn't -- in this study, they didn't even try to separate out NDMA separately, right?

A I don't know if they couldn't or didn't try. It wasn't separated.

Q Okay. But regardless of if they couldn't or didn't try or tried and it didn't work, the data that you're relying on is looking at exposure of -- exposure to nitrites, nitrates and nitrosamine all together, right?

MR. NIGH: Form objection.

THE WITNESS: Right.

BY MR. GALLAGHER:

Q And so you're not going to be able to separate out the specific impact of -- from this study, specific impact for NDMA risk for lymphoma, right?

A No, not specifically for NDMA.

Q You then look at the Straif study -- or you cite to the Straif study again. And you're -- this is back in your report on Page 23?

A Uh-huh.

Q Right?

A Yes.

Q And -- and you have the same criticism

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for Straif, that it was underpowered as you have for -- for other of the cancers, right?
A Yes.
Q But regardless, Straif does not provide evidence for an association of exposure to NDMA and occurrence of blood cancers, right?
A Let me just look at Straif again before I -- I mean, they had -- they had a small number of cases. They looked at nitrosamines. I mean, similar in structure, but not NDMA, per se. And they -- I mean, there was an increase in risk with lymphoma but not significant because of small number of cases.
Q Next -- and then you cite again to the Hidajat study, right?
A Right.
Q And you're looking at the data from Hidajat for lymphoma, leukemia and multiple myeloma, right?
A Right.
Q So really, Hidajat is the only study that you're citing to in support of your opinion with respect to exposure to NDMA and any association with blood cancers, right?
A Right.

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MR. NIGH: Form objection.
BY MR. GALLAGHER:
Q Moving on to Section 10.9 of your report on Page 24, which is "Lung Cancer"?
A Okay.
Q So, for lung cancer, you cite to a De Stefani article?
A Uh-huh.
Q Right?
A Is there an exhibit?
Q It's a 2009 article that you cited to. That's what Citation Number 44 is.
A Right. Are you going to upload it, or am I just going to look at it here?
MR. GALLAGHER: Can we go ahead and mark that.
(Whereupon, Exhibit 23 was marked for Identification.)
MR. GALLAGHER: So that's Exhibit 23, and I'm also going to mark now as Exhibit 24 a De Stefani article from 1998.
(Whereupon, Exhibit 24 was marked for Identification.)
BY MR. GALLAGHER:
Q Do you have Exhibit 23 in front of you?
A Yes.
Q Okay. This -- this study was looking at meat intake and risk of lung cancer; is that right?
A I just want to note, make sure that this is the one that I cite.
Q Okay. We had some confusion there to, so that's why I'm going to pull up the other one.
A The meat intake one, I don't think it provided NDMA levels. I don't think that I used that. I think I used the other one.
Q Okay. If you look in your report, looking at Page 24, under "Lung Cancer," you say, "A study by De Stefani examined the risk of lung cancer among subjects exposed to different levels of NDMA through diet."
Do you see that, right?
A Right. I think that should be another De Stefani. It probably got mixed up.
Q Okay. But if we go to --
A If we go to the '96 article.
Q Okay. But if we go to Page 38 of -- of your report, listing the references?
A Uh-huh.

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Q The -- Reference 44 you're citing to this article "Meat Intake, Meat Mutagens and Risk of Lung Cancer in Uruguayan Men."
THE COURT REPORTER: I'm sorry. I'm sorry. Excuse me.
MR. GALLAGHER: Do you need me to repeat the question with it?
THE COURT REPORTER: No.
MR. GALLAGHER: Do you need Dr. Etminan to repeat his answer?
THE COURT REPORTER: Yes.
BY MR. GALLAGHER:
Q I'll repeat the question.
So Dr. Etminan, here in your report, Reference 44 is this De Stefani article from 2009 titled, "Meat Intake, Meat Mutagens and Risk of Lung Cancer in Uruguayan Men," right?
A Right. And I believe that that should actually be another -- should be replaced by another De Stefani. It got mixed up, some so the De Stefani data that I included is from the De Stefani '96 in "Cancer Epidemiology" --
THE COURT REPORTER: What markers?
THE WITNESS: "Cancer Epidemiology Biomarkers and Prevention."

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THE COURT REPORTER: Thank you.
BY MR. GALLAGHER:
Q But you agree with me that this 2009 article does not separately evaluate levels of NDMA, right?
A Right.
Q Okay.
MR. GALLAGHER: We'll mark as Exhibit 24 a 1996 De Stefani article. Let me know when that shows up in your chat.
THE WITNESS: Sorry. That should be De Stefani 2000 -- is it -- exhibit which number?
BY MR. GALLAGHER:
Q Exhibit 24. It should be coming shortly.
A Right. 24, okay.
Q Have you got it?
A Yes.
Q Okay. So is this -- this is the article that you meant to refer to?
A Yes.
Q That's in Reference 44 from your report?
A Yes.

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Q Okay. And the title of this -- this is an older article than Exhibit 23 that we were just looking at, right?
A That's right.
Q And this is entitled, "Dietary Nitrosodimethylamine and the Risk of Lung Cancer: A Case Control Study from Uruguay," right?
A That's right.
Q Okay. So this -- this was a dietary study, right?
A Yes.
Q And this is subject to the same limitations of the other dietary studies that we've talked about in terms of -- errors in filling out the dietary questionnaire would be one, right?
A Well, again, dietary questionnaires, usually, the error is differential -- non-differential -- pardon me, non-differential. Here they do show a risk, but it is a dietary questionnaire study. So generally speaking, it could have limitations, but I don't -- I mean, I can't even think of a specific reason why the -- a specific reason as to why they put limitations in terms of the questionnaire would, you know, would affect the results. But generally speaking, all

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dietary studies could have --
THE COURT REPORTER: Could have what?
THE WITNESS: Limitations.
THE COURT REPORTER: Thank you.
BY MR. GALLAGHER:
Q Okay. And this is a case control study, correct?
A Yeah. Yeah.
Q Would you consider this a retrospective study?
A Yes.
Q Is there a potential for recall bias for the dietary questionnaire?
A There could be. In all dietary studies that's a possibility.
Q Okay. And is a part of -- a part of what leads to that recall bias could be that the cases for those with lung cancer feel more invested in identifying what the -- what led to their diagnosis, whereas the controls are not in the -- in the same type of a situation, right?
THE COURT REPORTER: I'm sorry. What was the objection?
MR. NIGH: Form objection.
THE COURT REPORTER: And was there an

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answer?
THE WITNESS: I said that it's possible.
BY MR. GALLAGHER:
Q Okay. Moving on in your report, you next cite to a study by Goodman?
A Yes.
Q One more thing. Back in your report, when you're discussing the De Stefani article --
MR. GALLAGHER: If we can highlight that section. Yup.
BY MR. GALLAGHER:
Q And you talk about, "The study identified 320 cases of lung cancer and matched them to 320 controls," right?
A Yeah.
Q And -- and then you say, "After adjusting for important confounding variables, including pack-years of smoking and history of lung cancer," and you go on to talk about the data.
A Uh-huh.
Q So you agree that smoking and past history of cancer are important confounding variables, right?
A Yes. And if you have the data, if

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you -- have the data available, it should be adjusted for. I think what we talked about, in a different sort of context, today is that lack of an unmeasured confounder doesn't always mean that the results would be biased. But if you have a confounder that is important and it's been collected, then by all means, it should be --

THE COURT REPORTER: It should be what?

THE WITNESS: Controlled for.

BY MR. GALLAGHER:

Q And so for studies that don't control for these important confounding variables, that is a limitation of those studies, right?

A It is a limitation, but again, we have -- we have sort of techniques, too, that we can use to simulate the data and see how it affects -- it would affect the results. And it is a limitation, but it does not necessarily mean that the study should not be believed in. Because, as I -- as I mentioned a number of times, a lack of an unmeasured confounder doesn't always lead to, you know, biased results. It depends on a number of criteria and situations on the confounding.

Q Right. But you don't know if -- if

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any one given confounding variable -- actually, unmeasured confounding variable, actually did bias the results, right?

MR. NIGH: Form objection.

THE WITNESS: Exactly and precisely, no, unless you have the data.

BY MR. GALLAGHER:

Q Okay. And when you have multiple unmeasured confounding variables, that just complicates it even more in terms of whether one or more of those multiple unmeasured confounding variables actually bias the results, right?

MR. NIGH: Form objection.

THE WITNESS: If -- if those -- a lot of times, these variables that, you know, are mentioned as confounders are not true confounders. They are risk factors as we talked about it. So in -- in a situation of risk factors, I -- I don't think again, lack of measuring for a risk factor only affects the precision around the effect size. It -- usually minimally, doesn't change the direction. So to answer your question, yes, but a lot of times, these are not really unmeasured confounders. They are just risk

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factors. Yeah.

BY MR. GALLAGHER:

Q Okay. Moving on in your report, now you cite to a study by Goodman?

A Yes.

MR. GALLAGHER: And let's go ahead and mark this. This is going to be Exhibit 25. Let me know when you have it.

(Whereupon, Exhibit 25 was marked for Identification.)

THE WITNESS: I have it.

BY MR. GALLAGHER:

Q So this article, Exhibit 25, is titled, "High Fat Foods and the Risk of Lung Cancer," right?

A Yes.

Q So this study is focusing on the effect of dietary cholesterol and dietary fat on lung cancer risk, right?

THE COURT REPORTER: And dietary what?

MR. GALLAGHER: Dietary fat.

THE WITNESS: Okay.

BY MR. GALLAGHER:

Q And this was a diet history survey, right?

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A Yes.

Q And, in fact, in almost -- this is a diet history survey, and do you understand that -- so in terms of a diet history survey, that's different from a food frequency questionnaire; is that right?

MR. NIGH: Form objection.

THE WITNESS: Let me just -- can I just read it for a few minutes?

BY MR. GALLAGHER:

Q Sure.

MR. GALLAGHER: Can we go off the record for a minute while he -- to give him time to review?

THE VIDEOGRAPHER: The time is now 4:25. We're going off the record.

(Whereupon, a short break was taken.)

THE VIDEOGRAPHER: The time is now 4:27. We're back on the record.

BY MR. GALLAGHER:

Q Okay. So this -- this study uses diet history survey, right?

A Yes.

Q Okay. And, in fact, in -- in many instances, the subject of the study wasn't

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available, and so they actually used -- did an interview with a surrogate in order to collect the historic information on diet history, right? Maybe -- go ahead.

A Yes, I mean, in a lot of dietary studies, especially when the patients are elderly, it's usually a family member who helps to complete the questionnaire. So -- I don't think this is that much of a difference in, sort of, a step involving the survey versus other dietary questionnaires that we see.

Q Okay. If we turn to Page 289 of the Goodman article?

A Yes.

Q And here, this is the section describing subjects and methods. On the left-hand side, the paragraph second from the bottom starts, "In some instances." And this is describing --

A Yeah.

Q -- why in some circumstances they obtained surrogate interviews from the spouse or next of kin, right?

A Yeah.

Q And for this study, surrogate interviews were conducted for 29 percent of the

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cases, but only 7 percent of the controls, right?

A Right.

Q So there's an unequal -- there's an unequal distribution of surrogate interviews for the cases versus for the controls, right?

A Right. But you're -- I think you're automatically assuming that the unequal distribution leads to, say, again, measurement error on the part of the cases. And we -- we don't know if that's the case. I mean, it could, in fact, because it's --

Q Sure.

A -- it could actually improve accuracy. We don't know. All we know is that there is a difference in percentage of those who used the surrogate versus those who didn't.

Q Okay. So we have already talked about one of the -- and it's just an inherent limitation of dietary studies, is the potential for inaccurately reporting in terms of foods that the subject does eat, the food frequency.

A Generally speaking, yes --

MR. NIGH: Hold on. Form objection. Form objection.

Go ahead. You can answer.

THE WITNESS: Generally speaking, I

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think it's -- we talked about this already.

BY MR. GALLAGHER:

Q Okay. And there certainly is a possibility that a surrogate will have a different level of accuracy than the subject themselves in recalling foods that the subject has -- has typically eaten, correct?

MR. NIGH: Form objection.

THE WITNESS: It's -- it's possible.

BY MR. GALLAGHER:

Q And especially where the -- the percentage of surrogate interviews for the cases is different from the percentage of surrogate interviews for the controls. Any difference in accuracy of the surrogates and the actual subjects, both see the data, right?

MR. NIGH: Form objection.

THE WITNESS: Again, if you're assuming that there are measurement errors with the cases versus the controls. If that would be the case, then, yes.

BY MR. GALLAGHER:

Q Okay. And just to be clear, I'm not just asking about differences in recall of cases versus controls.

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I'm asking about, there can be differences in -- in recall of foods that were typical in a person's diet if the person answering the question is the subject themselves versus if the person answering the questions is a surrogate for the subject, right?

A Yes.

Q Back to your report on Page 24, the second paragraph of "Lung Cancer," that is referring to the Goodman study.

A Uh-huh.

Q So after discussing the odds ratio, you say, "One limitation of Goodman is that it is unclear how duration of exposure to nitrosamines was assessed."

Do you see that?

A Yes.

Q You agree with me that duration of exposure to nitrosamine is a factor that has to be considered in terms of evaluating them if there's any potential risk factor, right?

A Yes. And, again, that's why I'm also -- in forming my opinion, I'm also relying on the Hidajat study, which measured NDMA exposure through inhalation, which would have a direct effect

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in this specific -- for this specific cancer on the lung.
Q. Okay. And then in your report you next cite to the Loh study, which we have looked at and discussed previously. The Loh study reports a relative risk of 1.05, a 95 percent confidence interval of 0.88 to 1.24, correct?
A. Yes.
Q. So you would agree with me that the Loh study does not provide evidence of an association between NDMA exposure and risk of lung cancer, right?
A. Correct.
Q. Okay. Going back to the odds ratios for -- from the Goodman study, for the first one which is intake of NDMA in men, the confidence interval is 1.7 to 6.2, right?
A. Yes.
Q. Would you consider that confidence interval to be imprecise?
MR. NIGH: Form objection.
THE WITNESS: No. Imprecise, we usually mean imprecise when it crosses 1 and goes beyond 1, and -- and -- so that the lower bound goes from, say, minus 1 -- or minus 1,

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and the upper bound goes to greater than 1. That's what they call imprecise.
If it's -- if it's some sort of skew to the right from 1.1 or higher, as it is in this case, we wouldn't say that's imprecise.
BY MR. GALLAGHER:
Q. Okay. Well, if there's no association, you would expect the confidence interval to go below 1 and above 1, correct?
A. I'm sorry. Can you clarify the question?
Q. If there's no association between the exposure and the outcome, you would expect the confidence interval, the lower bound to be below 1 and the upper bound to be above 1, correct?
A. Well, that's -- again, I think we talked about this. So that would be an inconclusive. I wouldn't say no association. If the effect size is greater than 1, but the confidence intervals are as wide as you just mentioned, that would be an inconclusive sort of a result rather than no association.
Q. Okay. I guess, I didn't say the confidence intervals were wide. I just said if there's no association, you would expect the lower

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bound of the confidence interval to be below 1 and the upper bound of the confidence interval to be above 1, right?
A. Yes. So, again, what you're portraying the confidence interval that's -- that crosses 1. So it goes either way, and, again, that fits the -- again, we don't have specific numbers here. But that usually fits the definition of imprecision or uncertain results, not necessarily negative results, uncertain results. Or inconclusive results.
Q. Okay. If you had a study that was extremely well-powered, and you -- you actually did observe from the data a relative risk of 1.0, and the confidence interval was 0.98 to 1.02, are you telling me that you would consider that confidence interval to be imprecise?
MR. NIGH: Form objection.
THE WITNESS: No. But, again, in your example, you didn't -- you didn't specify numbers with the numbers that you're -- you're giving me now, which -- which seem to be very tight. And, again, if -- if this is a non-biased study, a perfectly designed study, then that would be a no association.

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BY MR. GALLAGHER:
Q. Okay. And so this discussion about imprecise confidence intervals are when it's -- the lower bound is below 1 and the upper bound is above 1, that's not actually a measured determination of whether the confidence interval is precise or not, right?
A. Again, it -- it depends on the -- what the confidence interval is -- what the effect size is, and what the confidence interval is around that effect size. The example that you gave me fits your description, but if you have situations where you have, say, a relative risk of 4 and a very wide confidence interval, that does not -- that does not mean that there is no association. That means that that's an inconclusive study. So, again, I can't -- at least, I can't come up with a cookie-cutter definition. It depends on what the effect size is, and what the confidence interval around the effect size is.
Q. Okay. You can't come up with a cookie-cutter definition, but are there -- are there some sort of standards around what you're considering to be an imprecise confidence interval versus a precise confidence interval?

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A Yes, so again --
MR. NIGH: Form objection.
Go ahead. You can answer.
THE WITNESS: If the relative risk of a study is 4 and the 95 confidence interval is from .3 to 15, that would be an inconclusive study. If the relative risk of the study is 4 and the -- and the lower bound starts from 1.8 to 6, that is not an imprecise study. That is -- that confidence interval, we call it a relatively tight confidence interval.
BY MR. GALLAGHER:
Q Okay. And then back to your report on Page 24, the next paragraph, you cite to the Hidajat study again, right?
A Yes.
Q And you cite to that, where the hazard ratio reported by Hidajat for exposure and NDMA having a potential association of lung cancer with the hazard ratio being 1.70, right?
A Yes.
Q And as we have discussed, the Hidajat study is an occupational study in the rubber industry in the UK where the exposure to NDMA was primarily through inhalation, not oral, right?

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A Yes.
Q And as I think you just mentioned, there's perhaps some plausibility to why inhalation of something may have an impact that the lung -- that oral ingestion would not, right?
A Can you repeat that last question, please?
Q Sure.
I think you had referenced in one of your earlier answers that you can understand why inhalation of a substance could -- could have some sort of an impact on the lungs, right?
A Yeah. I mean, inhaling a carcinogen would have probably more of a -- would -- would have -- would be able to impose more of its carcinogenic effect because it's directly affecting that organ. But eventually, it will be -- it will be absorbed systemically over time. It's just that the first organ its seeing is the lungs because it's going through inhalation. So it may affect the organ -- the lungs more, but over time, it will be systemically absorbed and affect potentially other parts of the body.
Q Okay. And as we talked about, workers in rubber factories are not just inhaling NDMA.

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They're inhaling all sorts of things, including rubber dust, rubber fumes, benzine. There's all sorts of things that are --
MR. NIGH: Hold on. I'd like to object here. This is about the 20th plus time that I've heard this same question, you know. I think there was an instruction not to be cumulative. We have been patient. We have let the cumulative questions come on multiple topics, but this is the point as to which it's becoming very much overly cumulative. It's the same question over and over on the same topic. And I could come up with probably 20 examples right now of the same question being asked.
You know, at this point, I -- you know, I would caution the counsel that they're -- I think that counsel may be thinking they have 10 hours of record time. I do not believe that's the case. I think that there were strings that were attached and things that were said that -- you know, in terms of seven hours and when the exception may apply. And, frankly, I don't think that that exception is applied here.
So, again, I would object. This has

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become completely overly cumulative. And I would rest on the federal rules of seven hours saying that none of the exceptions have been met for the judge's ruling on 10 hours in this case.
You can answer.
THE WITNESS: Sorry. I forgot what the question was.
MR. GALLAGHER: You know, I think the judge was -- was very clear in his ruling that we had 10 hours, and was equally as clear during the Hecht deposition and unhappy when he was bothered in the middle of dinner and the deposition had not -- was not anywhere close to -- to 10 hours. So moving on.
BY MR. GALLAGHER:
Q Dr. Etminan, on Section 11 in your expert report?
A Yes.
Q This is addressing epidemiologic studies of valsartan-containing NDMA and cancer, right?
A Yes.
Q In these studies, they are actually addressing the exposure -- well, let me step back

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for a minute.
MR. GALLAGHER: Let's mark as Exhibit 26, the Pottegard study, and as Exhibit 27 the Gomm, G-o-m-m, study.
(Whereupon, Exhibit 26 was marked for Identification.)
(Whereupon, Exhibit 27 was marked for Identification.)
BY MR. GALLAGHER:
Q Let me know when those two exhibits show up, Exhibit 26 and 27.
THE WITNESS: Sorry. I got disconnected and got reconnected. There is nothing in the -- okay, I see it now.
BY MR. GALLAGHER:
Q Okay. You have Exhibit 26 as the Pottegard study, right?
A Yeah.
Q And Exhibit 27 is that there also, the Gomm study?
A I just got 26 for now. Yes.
Q So both of these studies are evaluating the exposure that's actually at issue in this litigation, right, which is exposure to valsartan that contains some small amount of NDMAs

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of impurity, right?
A They're not -- I disagree. They're not -- they're not quantifying the NDMA valsartan. They are only looking at valsartan tablets and doses.
Q The exposure that they're evaluating is -- so the title of the Pottegard study is "Use of N-nitrosodimethylamine (NDMA) Contaminated Valsartan Products and Risk of Cancer: Danish Nationwide Cohort Study," right?
A That -- that is the title, but if you read the study -- the exposure that we're here today to talk about is NDMA and its risk of cancer, and so the study should address the amount of NDMA in valsartan and its risk with cancer. What it does, though, is look at valsartan tablets that have some NDMA in it, in them, we don't know how much.
And with respect to Pottegard, we -- we are not even sure if the -- the control valsartan group didn't have NDMA in those formulations.
So there is definitely measurement error going on in quantifying -- appropriately quantifying NDMA in valsartan along with other limitations.
Q Why do you say that there's definitely

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measurement error?
A Because NDMA levels vary in different batches or different types of valsartan. But there are many different generic valsartan products, and they may have different levels of NDMA in them. So higher levels may put somebody at a higher risk of cancer, and this study did not look at that, which I think is an important distinct that should be looked at.
And also because the study was done early on, it turns out that some of the control group, which they -- they thought did not have NDMA in them probably did have NDMA in them as well. So there is again an error in measurement between the two groups. So that is -- that is the limitation of the, you know, measurement error portion of this study.
Q Okay. So am I understanding right, they would have to know the amount of NDMA that each of the subjects was actually exposed to to evaluate whether there actually is a risk of these cancers, from that literature?
A They would have to -- they would have to categorize -- have had to categorize the different levels of -- hello?

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MR. GALLAGHER: I can hear you. Does somebody else need to mute, maybe?
THE WITNESS: Yeah, there's an echo.
They should have -- maybe they couldn't, but the -- the right thing to do is to categorize different NDMA levels in these valsartan tablets and categorize them to say: High, medium and low dose. And then follow patients for more than the amount of time, I think it's three years, I believe, that they did, to make sure that they are at risk of developing cancer.
And then also make sure that the control group does not have any NDMA in those -- in those batches. And they can also make sure there's no switching going on, because, again, patients take these drugs from their pharmacy. And they don't really specify which generic formulation they get. So there could be switching between patients, and they could be switching between the doses of NDMA over time. So all of those limitations I think probably led to the negative results.
BY MR. GALLAGHER:
Q Okay. You do agree with me that the

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Pottegard study reports a negative result in terms of any association between exposure to NDMA as an impurity in valsartan and --
A Well, again, negative results with the caveat of a number of limitations.
Q Okay. And among those -- among those limitations that you've identified is the people conducting the study would need to somehow quantify the amount of NDMA to which the subjects were actually exposed in order to evaluate that potential association of exposure to NDMA as an impurity of valsartan with cancer?
A Right. I make sure that those -- those patients are taking these higher levels of NDMA for at least a specific period of time to allow the cancer process to sort of form and be diagnosed.
You know, if somebody takes the drug for three months and then leaves the study, that -- that is not a good follow up for this study. You need long follow up. You need minimal switching. You need specific NDMA dosing information for the subjects, and you need to make sure that the control group are all clean valsartan users, and there's no NDMA in them as well.
Q Okay. Moving on to the Gomm study, do

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you have that now, Exhibit 27, I believe?
A Yes.
Q And you're addressing the Gomm study on Page 26 of your report. From your perspective, does the Gomm study, you know, essentially have, from your perspective, the same limitations as we just discussed for the Pottegard study?
A Yes, I would again --
MR. NIGH: Hold on. Hold on. Let me object. Form objection.
You can answer, Dr. Etminan.
THE WITNESS: Yes. Again, just like Pottegard, there's no specification of the NDMA content in the valsartan users, and I think they actually say possible or probable contamination. So there's a feeling of uncertainty as to, you know, whether, say, for example, the control group had any NDMA or did not have any NDMA. There's no discussion of what if people switch between the, you know, different doses which could have had different NDMA levels.
And then there is the problem of only a three-year follow up, which for a cancer is quite inadequate. And there's also some

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evidence of selection bias as well.
BY MR. GALLAGHER:
Q Okay. And with respect to -- just discussing -- discussing the limitation you have identified of -- of time to follow up, you understand that these -- these products were on the market only relatively recently. So between approximately 2014 and 2018, there's -- there's not, at the moment, an opportunity for any longer follow up, right?
MR. NIGH: Form objection.
THE WITNESS: Yes. I mean, that is the problem. But that doesn't take away from the fact that -- I mean, if you can't do this study, you shouldn't do it. You should wait until you have adequate follow up. You cannot do sort of a -- you cannot disregard an important part of this study design, which is adequate follow up, because there just simply isn't enough data. I mean, they could have waited until more data is accumulated before they actually did this study.
BY MR. GALLAGHER:
Q It's not that they necessarily shouldn't do the study, but it's just acknowledging

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that there's no other data. There's no longer term follow up data that's available right now?
A Okay.
MR. GALLAGHER: I want to be sensitive to the court reporter. We have been going for an hour, when she asked that that be how far we go, so can we -- can we go off the record now?
THE VIDEOGRAPHER: The time is now 4:59. We're going off the record. This ends Media Unit Number 6.
(Whereupon, a short break was taken.)
(Whereupon, the deposition concluded at 4:59 p.m.)

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DEPOSITION REVIEW
CERTIFICATION OF WITNESS

ASSIGNMENT REFERENCE NO: 4772261
CASE NAME: Valsartan
DATE OF DEPOSITION: August 24, 2021
WITNESS: MAHYAR ETMINAN, Ph.D.

In accordance with the Rules of Civil Procedure, I have read the entire transcript of my testimony or it has been read to me.

I have listed my changes on the attached Errata Sheet, listing page and line numbers as well as the reason(s) for the change(s).

I request that these changes be entered as part of the record of my testimony.

I have executed the Errata Sheet, as well as this Certificate, and request and authorize that both be appended to the transcript of my testimony and be incorporated therein.

_____ _____
Date Mahyar Etminan

Sworn to and subscribed before me, a Notary Public in and for the State and County, the referenced witness did personally appear and acknowledge that:

They have read the transcript;

They have listed all of their corrections in the appended Errata Sheet;

They signed the foregoing Sworn Statement; and

Their execution of this Statement is of their free act and deed.

I have affixed my name and official seal this_____day of_____, 20_____,

_____
Notary Public

_____
Commission Expiration Date

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DEPOSITION ERRATA SHEET

Page Line From to

SIGNATURE:_____DATE:_____
MAHYAR ETMINAN

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CERTIFICATE

I, Jamie I. Moskowitz, a Shorthand (Stenotype) Reporter and Notary Public, do hereby certify that the foregoing Deposition, of the witness, MAHYAR ETMINAN, taken at the time and place aforesaid, is a true and correct transcription of my shorthand notes.

I further certify that I am neither counsel for nor related to any party to said action, nor in any way interested in the result or outcome thereof.

IN WITNESS WHEREOF, I have hereunto set my hand this 1st day of September 2021

Jamie Ilyse Moskowitz
License No. XI01658

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Federal Rules of Civil Procedure

Rule 30

(e) Review By the Witness; Changes.

(1) Review; Statement of Changes. On request by the deponent or a party before the deposition is completed, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which:

(A) to review the transcript or recording; and

(B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them.

(2) Changes Indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30(f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period.

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VERITEXT LEGAL SOLUTIONS
COMPANY CERTIFICATE AND DISCLOSURE STATEMENT

Veritext Legal Solutions represents that the foregoing transcript is a true, correct and complete transcript of the colloquies, questions and answers as submitted by the court reporter. Veritext Legal Solutions further represents that the attached exhibits, if any, are true, correct and complete documents as submitted by the court reporter and/or attorneys in relation to this deposition and that the documents were processed in accordance with our litigation support and production standards.

Veritext Legal Solutions is committed to maintaining the confidentiality of client and witness information, in accordance with the regulations promulgated under the Health Insurance Portability and Accountability Act (HIPAA), as amended with respect to protected health information and the Gramm-Leach-Bliley Act, as amended, with respect to Personally Identifiable Information (PII). Physical transcripts and exhibits are managed under strict facility and personnel access controls. Electronic files of documents are stored in encrypted form and are transmitted in an encrypted fashion to authenticated parties who are permitted to access the material. Our data is hosted in a Tier 4 SSAE 16 certified facility.

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